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Original Research Article

Role of bronchoalveolar lavage, transbronchial needle aspiration with bronchial biopsy correlation in lung tumours and immunohistochemistry wherever required

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ABSTRACT

Background: Lung cancer is most frequently diagnosed major cancer in the world and the most common cause of cancer mortality worldwide. It comprises about 17% of the total new cancer cases in males and 23% of the total cancer deaths. The objectives of this study were to compare bronchial biopsy, BAL and TBNA in diagnosing lung malignancies and IHC wherever required.
Methods: The study was conducted at Sher-i-Kashmir Institute of Medical Sciences Srinagar, India in the department of Pathology. It was a prospective study over a period of 1½ years from June 2015 to December 2016. All patients clinically/ radiologically suspected of lung malignancies who presented between June 2015 to December 2016 and underwent bronchial biopsy, BAL (washings) and TBNA were included in the study. The study included only those cases where BAL, TBNA and bronchial biopsy were done simultaneously.
Results: Out of a total 117 clinically suspected cases of lung cancer, tumor was found in 103 cases (103/117) by biopsy, 51 cases by BAL (51/117) and 64 cases by TBNA (64/117). The total number of false positive cases and false negative cases by BAL were 6 and 58. Sensitivity of BAL was found to be 43.69% and specificity 57.14%. The total number of false positive cases and false negative cases by TBNA were 7 and 46. Sensitivity and specificity of TBNA was found to be 55.34% and 50.0%.
Conclusions: Thus, in the present study yield of diagnosis was highest with the bronchoscopic biopsies and in maximum number of cases with a sensitivity of 88.034%, and specific histologic diagnosis was made by biopsies and IHC only. Though BAL and TBNA were inferior to bronchial biopsy in diagnosing lung malignancies but these were effective for peripheral lung malignancies and when the patient was at risk of haemorrhage.

Keywords: Bronchial biopsy, Bronchoalveolar lavage, Immunohistochemistry, Lung carcinoma, Transbronchial needle aspiration

INTRODUCTION

Lung cancer is most frequently diagnosed major cancer in the world and the most common cause of cancer mortality worldwide.[1] It comprises about 17% of the total new cancer cases in males and 23% of the total cancer deaths.[2] The incidence is increasing dramatically in women and lung cancer has surpassed breast cancer as a leading cause of cancer death in women. Cancer of the lung most often occurs between age 40 and 70 years with a peak incidence in the fifties and sixties. Several studies however have demonstrated that early detection, localization and aggressive treatment of lung cancer results in five year survival rate of 70 to 80%.[3] For early

diagnosis different diagnostic modalities are available like radiology, bronchoscopy, bronchial biopsy, exfoliative cytology, brushing, washing, sputum cytology and FNAC. It is not possible to perform all techniques in each patient because each has specific advantages and disadvantages. However, their combined use yields the best results.[4] Approximately 80-85% of lung cancer deaths are attributed to smoking.[5]

The diagnostic sensitivity of bronchial biopsy in diagnosing lung malignancies ranges from 65-83%.[6,7] 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 visible tumors than in those with tumors not visible endoscopically.[8]

The sensitivity of BAL varies between 14-76% in various studies reported. It is a valuable diagnostic tool in detecting peripheral primary pulmonary malignant neoplasm.[9] BAL is an easily performed and well tolerated procedure that is used in routine assessment of patients for carcinoma lung. It also helps tamponade any bleeding that may have occurred as a result of biopsy. The technique of TBNA was developed in early eighties to obtain cytological and histological samples from the hilar or mediastinal lesions with flexible transbronchial needles introduced through tracheal and bronchial walls.[10] Various publications have highlighted the utility of this TBNA procedure in the diagnosis of endobronchial and peripheral lesions, even in the absence of endo bronchial disease.[11]

The procedure is safe, inexpensive and can be performed easily during a routine diagnostic bronchoscopy obviating the need for another surgical procedure for staging. In order to improve the yield of bronchoscopy for diagnosis of peripheral masses, TBNA technique is being employed in several centres.[2-4] TBNA has been shown to be useful in the diagnosis of primary pulmonary lesions.[12] in addition to its use as a staging procedure in patients with lung cancer and mediastinal adenopathy.[13] There is still however disagreement as to the value and reliability of BAL and TBNA in comparison with histology for the diagnosis of malignancy.

The present study was therefore undertaken to ascertain the role and diagnostic utility of BAL, TBNA and bronchial biopsy with IHC wherever required in diagnosing patients with bronchogenic carcinoma. A total of 47 cases were taken for IHC- Pan-Ck, P63, chromogranin, synaptophysin and TTF1.

METHODS

The study was conducted at Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Kashmir India in the department of Pathology. It was a prospective study over a period of 1½ years from June 2015 to December 2016.

Inclusion criteria

- All histopathologic slides of Bronchial biopsies and cytology slides of TBNA and BAL received in the department were followed.

Exclusion criteria

- Bronchial biopsies, TBNA and BAL done for diseases other than cancer were excluded from the study.

Study population included 117 cases of BAL, TBNA and Bronchial biopsies.

The bronchial biopsies were examined, size and number of bits counted. The tissues were processed as per standard procedure. 4-5 mm thick sections were cut on microtome and stained by H and E stain. The stained slides were studied in detail microscopically. The diagnosis and typing of tumor were made according to World Health Organization's classification.[1] BAL fluid was received within half an hour along with relevant clinical details. It was immediately centrifuged for 5 minutes at 1500 rpm. Three slides were prepared from the sediment. Two of the slides were fixed in absolute alcohol, stained with Papanicolaou stain and one air dried was stained with MGG. These slides were studied microscopically, and diagnosis confirmed. The smears were grouped into malignant, suspicious/atypical and negative according to criteria described by Willis and Ramzy.[14] For both cytology and histology only specimen with unequivocal malignant features were considered to be positive.

The malignant cells were further typed as squamous cell carcinoma, small cell carcinoma, adenocarcinoma and undifferentiated. The sensitivity, specificity, accuracy, positive and negative predictive values were calculated by utilizing the predictive value model of Galen and Gambino.[15] A total of 47 cases were collected for IHC. Formalin fixed paraffin embedded blocks were retrieved and subjected to IHC for expression of Pan- Ck, P63, chromogranin, synaptophysin, and TTF1. Two 5 µ sections were cut from each study block and were stained with these markers.

Statistical analysis

All the statistical analysis was done by using the SPSS 19.0 version. All the comparison was done using Chi square method and diagnostic testing tools, p value of <0.05 was considered as statistically significant.

RESULTS

In this study on 117 clinically suspected cases of lung tumors, 103 cases were found to be malignant. The overall mean age of patients of primary lung cancer was 56.45 years with maximum number of cases between 61-

70 years. Out of total 117 cases males constituted 99 cases (84.6%) and females constituted 18 cases (15.3%) The male to female ratio was 5.86:1(Table 1), 83(71%) cases were smokers and 34(29.05%) cases were nonsmokers. Among smokers, 76(91.56%) cases were males and 7(8.43%) cases were females. The smoker to non-smoker ratio was 2.44:1. The smoker to non-smoker ratio among males was 3.30:1, whereas among females, it was 0.636. This study obtained a p value = 0.005 and we found that there is no statistical correlation between smoking and gender (Table 2).

Table 1: Age and sex wise distribution of cases. The overall mean age of patients of primary lung cancer was 56.45 years with maximum number of cases found between 61-70 years the male to female ratio was 5.86:1.

Age group	Males	Females	Total	%age
<20	1	0	1	0.9
21-30	2	1	3	2.6
31-40	5	6	11	9.4
41-50	19	7	26	22.2
51-60	31	1	32	27.4
61-70	31	3	34	29.1
71+	10	0	10	8.5
Total	99	18	117	100

Out of 117 cases of clinically suspected cases of lung cancer, 103 cases were diagnosed as tumors. On histopathology the lung tumors were categorized as squamous cell carcinoma 46 cases (44.7%), small cell carcinoma 21(20.4%) cases, adenocarcinomas 10(9.7%) cases, Poorly differentiated squamous cell carcinoma 7(7%) cases, Poorly differentiated carcinoma 5(5%) cases, Adenosquamous carcinoma 4(3.9%) cases, Large cell neuroendocrine cell carcinomas 3(2.9%) cases, Neuroendocrine Tumor (NET) grade -2 2(1.9%) cases, Poorly differentiated adenocarcinoma 2(1.9%) cases, Sarcomatoid carcinoma 2(1.9%) cases and NHL 1(1%) case (Table 3).

Cytohistological correlation of BAL, TBNA and Bronchial biopsy is shown in the (Table 4).

Table 2: Smoking history: the smoker to non-smoker ratio was 2.44:1. 83(71%) cases were smokers and 34 (29.05%) cases were non-smokers. Among smokers, 76(91.56%) cases were males and 7(8.43%) cases were females.

Gender	Males	Females	Total	Percentage
Smokers	76	7	83	71%
Nonsmokers	23	11	34	29.05%
Total	99	18	117	100%
(p value = 0.005)				

Table 3: Histopathological findings on bronchial biopsy.

Tumor type	No. of cases	%Age
Squamous cell carcinoma	46	44.7
Small cell NEC	21	20.4
Pd squamous cell carcinoma	7	6.79
Pd carcinoma	5	4.85
Adenocarcinoma	10	9.7
Adeno squamous carcinoma	4	3.9
Large cell NEC	3	2.9
Net-grade-2	2	1.9
Pd adenocarcinoma	2	1.9
Sarcomatoid carcinoma	2	1.9
NHL	1	1.0
Total	103	100

Table 4: Cytohistological correlation of BAL, TBNA and bronchial biopsy.

Tumor type	BAL		TBNA		Biopsy	
	Number	%age	Number	%age	Number	%age
Squamous cell carcinoma	10	19.60	23	35.93	46	44.7
Small cell NEC	3	5.88	13	20.31	21	20.4
Adenocarcinoma	1	1.96	8	12.5	10	9.7
Pd squamous cell CA	0	0.0	0	0	7	6.8
Pd carcinoma	31	60.78	13	20.31	5	4.9
Adeno squamous CA	0	0.0	0	0	4	3.9
Large cell NEC	0	0	0	0	3	2.9
Net-grade-2	0	0.0	0	0	2	1.9
Pd adenocarcinoma	0	0.0	0	0	2	1.9
Sarcomatoid carcinoma	0	0.0	0	0	2	1.9
NHL	0	0.0	0	0	1	1.0
“Atypical/suspicious”	6	11.76	7	10.93	--	--
Total	51	100.0	64	100.0	103	100.0

Table 5: Cytohistological correlation of lung malignancies with respect to BAL.

Diagnostic accuracy of BAL (n=117)			
Gold standard histopathology			
BAL for malignancy	Disease present	Disease not present	Total
Test positive	True positive 45	False positive 06	51
Test negative	False negative 58	True negative 08	66

In the present study of 117 clinically suspected cases of pulmonary malignancies, 45 cases were correctly diagnosed by BAL as malignant, 6 cases as suspicious/atypical which later on biopsy proved to benign lesions and were included in the false positive cases. Total number of negative cases diagnosed on BAL were 66 out of which true negative were 8 and false negative were 58 (Table 5). In this study on BAL sensitivity was found to be 43.69%, specificity was 57.14%, positive predictive value 88.24%, Negative predictive value 12.12%, Odds Ratio 1.034. In conclusion, BAL was positive in 45(38.46%) cases, biopsy was positive in 103(88.03%) cases. This study obtained a p- value of <0.001 and author found that biopsy was more accurate in diagnosing lung malignancies as compared to Bronchoalveolar Lavage (BAL). Which was found to be statistically more significant (p<0.001) (Table 6).

Table 6: BAL (Statistical analysis) BAL sensitivity was found to be 43.69 %, specificity was 57.14%, positive predictive value 88.24 %, Negative, Sensitivity predictive value 12.12%.

Parameter	Estimate lower-upper 95%cls (Wilson score)
Sensitivity 43.69%	(34.51, 53.32)
Specificity 57.14%	(32.59,78.26)
Positive predictive value 88.24%	(76.62, 94.51)
Negative predictive value 12.12%	(6.272, 22.14)
Like hood ratio of positive test 1.019	(0.695,1.491)
Like hood ratio of negative test 0.985	(0.792,1.225)
Odds ratio 1.034	
Cohen's kappa 0.00319	
(p<0.001)	

Table 7: Cytohistological correlation of lung Malignancies with respect to TBNA.

Diagnostic accuracy of TBNA (n=117)			
Gold standard histopathology			
TBNA for malignancy	Disease present	Disease not present	Total
Test positive	True positive 57	False positive 7	64
Test negative	False negative 46	True negative 7	53

In the present study of 117 clinically suspected cases of pulmonary malignancies, 64 cases were correctly diagnosed by TBNA as malignant, 7 cases as suspicious/atypical which later biopsy proved to benign lesions and were included in the false positive cases. Total number of negative cases diagnosed on TBNA were 53 out of which true negative were 7 and false negative were 46 (Table 7). Sensitivity of TBNA was found to be 55.34%, specificity was 50%, positive predictive value 89.062%, Negative predictive value 13.21%. In conclusion, TBNA was positive in 57(48.71%) cases. Biopsy was positive in 103(88.03%) cases. This study obtained a p- value of 0.027 and we found that biopsy was more accurate in diagnosing lung malignancies as compared to Transbronchial Needle Aspiration (TBNA). Which was found to be statistically significant (p=0.027) (Table 8).

Table 8: TBNA (statistical analysis) Sensitivity of TBNA was found to be 55.34%, specificity was 50%, positive predictive value 89.062%, negative predictive value 13.21%.

Parameter	Estimate lower-upper 95% CLS (Wilson score)
Sensitivity 55 .34%	(45.72, 64.58)
Specificity 50.0%	(26.8, 73.21)
Positive predictive value 89.062%	(79.1, 94.06)
Negative predictive value 13.21%	(6.548, 24.84)
Like hood ratio of positive test 1.107	(0.813, 1.506)
Like hood ratio of negative test 0.893	(0.646, 1.233)
Odds ratio 1.239	
Cohen's kappa 0.02423	
(p=0.027)	

Confirmation of diagnosis was done by immunohistochemistry (IHC); Different IHC markers in the form of P63, TTF-1, CK, SYP, CHG were done where diagnosis could not be made by biopsy only to confirm the final diagnosis. IHC was done on 47 cases.

So, in nutshell, out of 103 cases of lung tumors, after IHC was done, 57(55.34%) cases were proved to be squamous cell carcinomas, showing tumor cells arranged in clusters separated by fibrovascular septa, Dyskeratotic cells in (H and E), showing nuclear immunoreactivity for P63. Anthracotic pigment is also noted (Figure 1 and 2), 21(20.4%) cases as small cell carcinomas showing Malignant cells with nuclear molding, high N/C ratio, salt and pepper chromatin and scant amount of cytoplasm (Small cell carcinoma) (MGG Stain) (Figure 3), 15(14.56%) cases as adenocarcinomas showing nuclear immunoreactivity for TTF-1 and membranous immunoreactivity for (Pan-CK)- tumor cells forming glands, Anthracotic pigment is also noted Adenocarcinoma lung (Figure 4 and 5). 4(3.88%) cases as adenosquamous carcinomas, 3(2.91%) cases as large cell neuroendocrine carcinomas, 2(1.94%) cases as NET-Grade-2 (Figure 6 and 7) and 1(0.97%) case as NHL showing Tumor cells arranged in diffuse sheets (Figure 8) (Table 9 and 10).

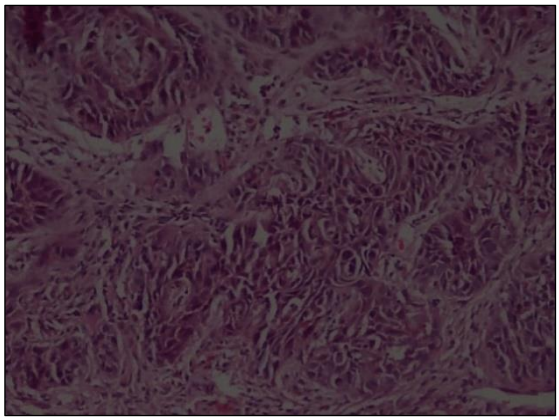

Figure 1: Photomicrograph showing tumour cells arranged in clusters separated by fibrovascular septa, Dyskeratotic cells in squamous cell carcinoma (H and E).

Table 9: Confirmation of diagnosis by (IHC); different IHC markers in the form of P63, TTF-1, CK, SYP, CHG were done where diagnosis could not be made by biopsy only to confirm the final diagnosis.

Histopathology* IHC			
Histopathology	IHC marker	No. of cases	Final diagnosis
Small cell neuroendocrine carcinoma	Synaptophysin (+)	15	Small cell neuroendocrine carcinoma
Large cell neuroendocrine carcinoma	Synaptophysin (+)	3	Large cell neuroendocrine carcinoma
Poorly differentiated squamous cell carcinoma	P63(+), Pan CK^+	7	Squamous cell carcinoma
Small cell nec carcinoma	Chromogranin (+)	6	Small cell neuroendocrine carcinoma
Poorly differentiated carcinoma	TTF1(+),CK^+	3	Adenocarcinoma
Poorly differentiated carcinoma	P63(+), PanCK^+	2	Squamous cell carcinoma
Adenosquamous carcinoma	P63(+), TTF1(+)	4	Adeno squamous cell carcinoma
Poorly differentiated adenocarcinoma	TTF1(+)	2	Adenocarcinoma
Neuroendocrine tumor-grade 2	Synaptophysin (+), CK^+	2	Neuro endocrinetumour-grade-2
Sarcomatoid carcinoma	P63(+), CK^+	2	Squamous cell carcinoma
Non-Hodgkin's lymphoma	Cd20(+)	1	Non -Hodgkin's lymphoma
Total		47	

Table 10: Final Diagnosis after IHC Confirmation: 57 cases were proved to be squamous cell carcinomas, 21 cases as small cell carcinomas, 15 cases as adenocarcinomas.

Final diagnosis after IHC	No. of cases	% age of cases
Squamous cell carcinoma	57	55.34
Small cell neuroendocrine carcinoma	21	20.4
Adenocarcinoma	15	14.56
Adenosquamous carcinoma	4	3.88
Large cell neuroendocrine carcinoma	3	2.91
NET Grade -2	2	1.94
NHL	1	0.97
Total	103	100

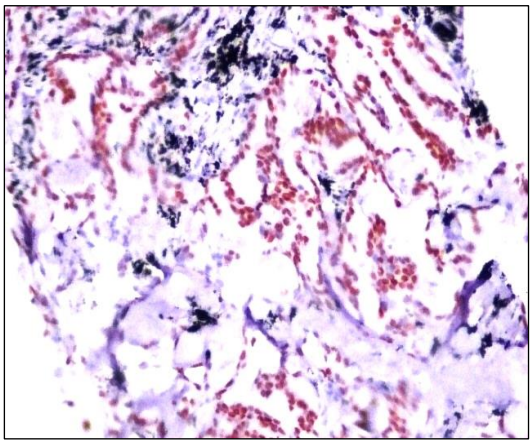

Figure 2: Photomicrograph (40x) showing nuclear immunoreactivity for P63-Squamous cell carcinoma. Anthracotic pigment is also noted.

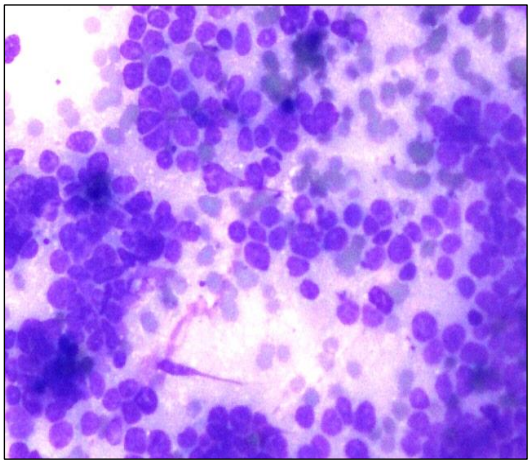

Figure 3: TBNA-Photomicrograph showing Malignant cells with nuclear molding, high N/C ratio, salt and pepper chromatin and scant amount of cytoplasm (Small cell carcinoma) (MGG Stain).

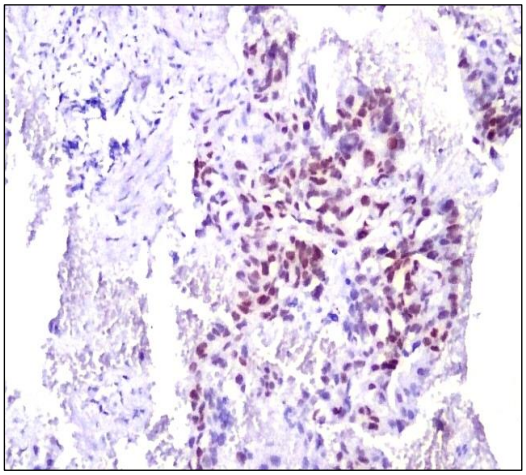

Figure 4: Photomicrograph (40X) showing nuclear immunoreactivity forTTF-1-Adenocarcinoma lung.

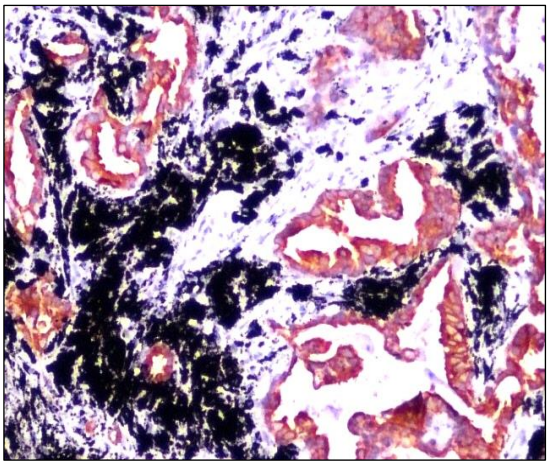

Figure 5: Photomicrograph (40x) showing membranous immunoreactivity for (Pan-CK)-adenocarcinoma (tumour cells forming glands, Anthracotic pigment is also noted the diagram)

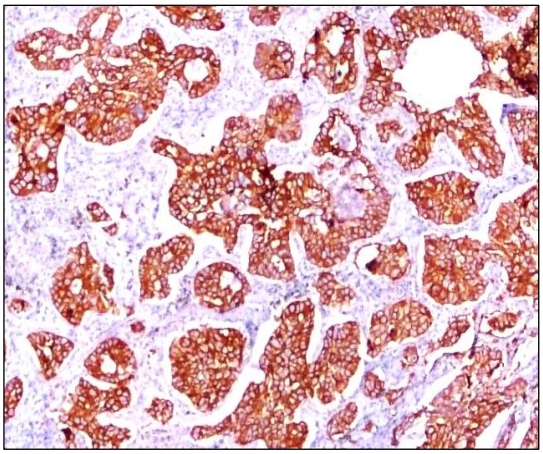

Figure 6: Photomicrograph(40X) showing cytoplasmic immunoreactivity for synaptophysin in well differentiated neuroendocrine tumour .

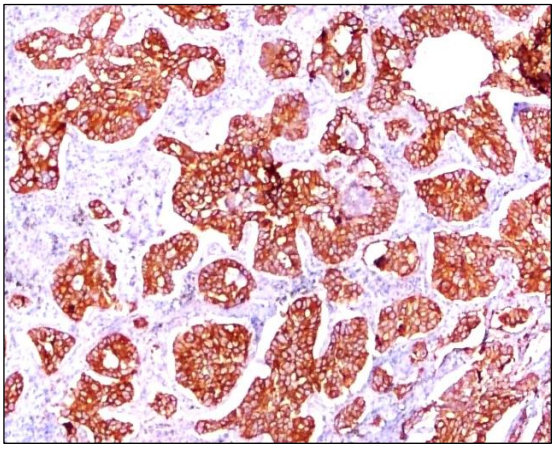

Figure 7: Photomicrograph (40X) showing tumour cells arranged in clusters, trabeculae and acini with membranous immunoreactivity for (Pan-CK) - Well differentiated neuroendocrine tumour.

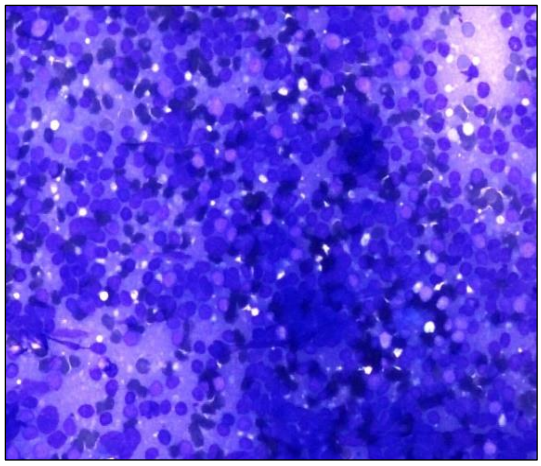

Figure 8: Photomicrograph of TBNA fluid -NHL (Tumour cells arranged in diffuse sheets).

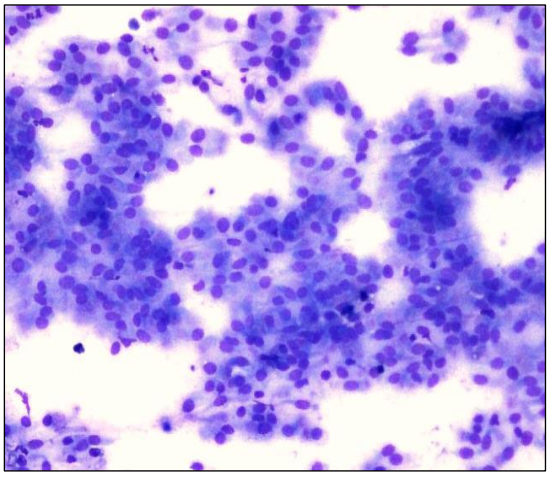

Figure 9: Photomicrograph of TBNA sample showing normal respiratory epithelial cells (MGG Stain).

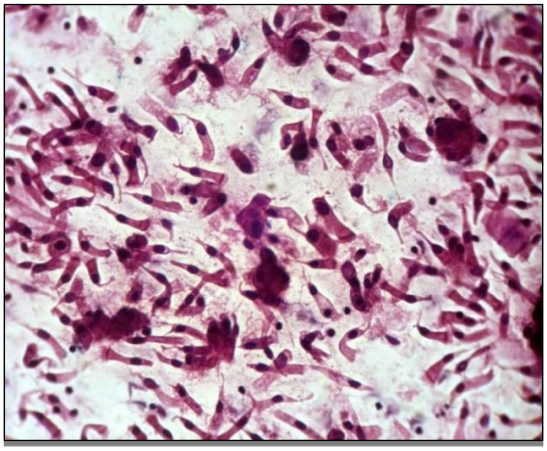

Figure 10: Photomicrograph of BAL showing normal respiratory epithelial cells (Papx400).

TBNA sample showing normal respiratory epithelial cells (MGG Stain) (Figure 9) and BAL sample showing normal respiratory epithelial cells (Papx400) (Figure 10).

DISCUSSION

Lung cancer is the leading cause of cancer related deaths in men and in women it has surpassed even breast cancer.[2] The increased number of the lung cancer deaths is mainly because it is detected at a late stage. Timely detection of disease plays an important role in the management and long-term survival of patients.[16]

Pulmonary cytology and histopathology are valuable tools in the diagnosis of lung malignancies. Fibreoptic bronchoscopy was introduced in 1968 as a diagnostic procedure.[17] Since then apart from sputum, different methods for obtaining satisfactory specimens have become available. BAL is considered as an effective tool for the diagnosis of this condition. It can provide diagnostic information in cases of primary and metastatic disease of the lung.

Though BAL is inferior to bronchial biopsy in diagnosing lung malignancies, it has certain advantages. It is a relatively safe procedure requiring less expertise, can be undertaken in peripheral lesions and in patients at risk of bleeding.[14]

In order to improve the yield of bronchoscopy for diagnosis of peripheral masses TBNA technique is being employed in several centres.[2-4] TBNA has been shown to be useful in the diagnosis of primary pulmonary lesions.[4] in addition to its use as a staging procedure in patients with lung cancer and mediastinal adenopathy.[10]

The present study was therefore undertaken to ascertain the role and diagnostic utility of BAL, TBNA and bronchial biopsy and IHC in diagnosing bronchogenic carcinoma. Out of 117 clinically suspected cases of lung malignancies, 103 cases (88.03%) were diagnosed by bronchial biopsyas lung cancer, the male to female ratio was 5.86:1. Faludi et al, (2004) found male to female ratio 6.22:1.[18] Out of 117cases, 83 were smokers and 34 non-smokers. The smoker to non-smoker ratio was 2.44:1. Our smoker to non-smoker ratio correlates well with Gupta D et al, (2001).[19]

In the present study lung malignancies were found in 103 cases (103/117) by bronchial biopsy. The most common type of lung cancer on biopsy was squamous cell carcinoma 55.33% (57 cases). The second most common type was small cell carcinoma 20.38% (21 cases), followed by adenocarcinoma 14.56% (15 cases), adenosquamous carcinoma 3.88% (4 cases), large cell neuroendocrine carcinoma 2.91% (3 cases), Neuroendocrine grade-2 tumour 1.94%(2 cases) and NHL 0.97% (1 case). In this study squamous cell carcinoma was the most common histological type in both the sexes. The relative frequency of small cell carcinoma and adenocarcinoma was higher in females as compared to males in this study.

Khan et al, (2006) found squamous cell carcinoma as the most common type of lung tumor (77.3 percent) followed

by small cell carcinoma (17.1 percent).[16] From the above we concluded that squamous cell carcinoma is the most common histological type of lung cancer as is seen in this study also. This study was also at variance to western literature where incidence of adenocarcinoma has surpassed squamous cell carcinoma.[20]

Of 117 clinically suspected cases of lung malignancies BAL was positive in 45 cases. Of these 10 cases (19.60%) were categorized by BAL as squamous cell carcinoma, 3 cases (5.88%) as small cell carcinoma, 1 case (1.96%) as adenocarcinoma, 31 cases (60.78%) as poorly differentiated carcinoma and 6 cases (11.76%) as suspicious/atypical. Gaur D S et al, (2007) found BAL was diagnostic in 17.9% cases (5/28) of squamous cell carcinoma, 7.1% cases (2/28) as small cell carcinoma and as many as 71.4% samples classified as poorly differentiated carcinoma.[21] Thus squamous cell carcinoma was the most common type of lung cancer diagnosed by BAL in the above studies which is comparable to this study. Comparision of clinical features and cell type pattern in different Indian Studies was done. In this we found that this study parameters were comparable to these studies as shown in the (Table 11).

Comparasion of statistical values on cyto-histological correlation in different Indian studies was done in relation to BAL and TBNA. In this we found this study parameters were comparable to these studies as shown in the (Table 12 and Table 13).

Table 11: Comparative clinical features and cell type pattern in different Indian studies.

Authors	Chokhani (1998) [22]	Koul et al, (2010)[23]	Bhat Nazia et al, (2016)[24]	Present study
Age group predominantly affected	61	55.77	58.6	56.45
Male to Female ratio	2.8	6.1:1	6.3:1	5.86:1
Smokers/Non-Smokers ratio	7.3	4.54:1	2.89:1	2.44:1
Squamous cell carcinoma	64%	67.5%	68.55%	55.33%
Small cell carcinoma	22%	20.8%	23.02%	20.38%
Adenocarcinoma	8%	3%	4.93%	14.56%
Large cell carcinoma	1%	1.08%	1.26%	2.91%
Undifferentiated carcinoma	4%	3.89%	0.7%	-

Table 12: Comparative statistical values on cyto-histological correlation in relation to BAL.

Author (year)	Place	No. of cases	Sensitivity (%age)	Specificity (%age)	Diagnostic accuracy (%age)
Gaur DS et al, (2007)[21]	India	196	39.4%	89.6%	71.40%
Bhat Nazia et al, (2016)[24]	India	902	35.5%	78.16%	42.43%
Present study (2017)	India	117	43.69%	57.14%	49.54%

Table 13: Comparative statistical values on cyto-histological correlation in relation to TBNA.

Author(year)	Place	No. of cases	Sensitivity (% age)	Specificity (% age)	Diagnostic accuracy (% age)
Gaur DS et al, (2007)[21]	India	51	62.5%	66.7%	63.3%
Tournoy (2009)[25]	Belgium	46	82%	-	-
Present study (2017)	India	117	55.34%	50.0%	54.701%

In the present study of 117 clinically suspected cases of pulmonary malignancies, 45 cases were correctly diagnosed by BAL as malignant, 6 cases as suspicious/atypical which later on biopsy proved to benign lesions and were included in the false positive cases. Total number of negative cases diagnosed on BAL were 66 out of which true negative were 8 and false negative were 58. The reasons for large number of false negative cases in this study were due to superadded inflammation in majority of the cases and non-representative material or hypocellular aspirates in rest of the cases.

In conclusion, BAL was positive in 45(38.46%) cases. Biopsy was positive in 103(88.03%) cases. This study obtained a p- value of <0.001and we found that biopsy was more accurate in diagnosing lung malignancies as compared to BAL. Which is found to be statistically more significant (p<0.001).

False positive can be mainly due to misinterpretation of the smears by the cytologist due to cellular changes in chronic inflammatory disorders.

In the present study false positive cases were because of misinterpretation of squamous metaplasia as suspicious. In rest of the cases it was due to misinterpretation of cuboidal alveolar cells as suspicious/atypical.

In the present study of 117 clinically suspected cases of pulmonary malignancies, 64 cases were correctly diagnosed by TBNA as malignant, 7 cases as suspicious/atypical which later on biopsy proved to benign lesions and were included in the false positive cases. Total number of negative cases diagnosed on TBNA were 53 out of which true negative were 7 and false negative were 46. The reason for large number of false negative cases in this study were due to superadded inflammation in majority of the cases and non-representative material or hypocellular aspirates in rest of the cases.

In conclusion, TBNA was positive in 57(48.71%) cases. Biopsy was positive in 103(88.03%) cases. This study obtained a p-value of 0.027 and Author found that biopsy was more accurate in diagnosing lung malignancies as compared to TBNA which was found to be statistically significant (p=0.001).

Immunohistochemistry (IHC)

Out of 103 confirmed cases of lung malignancies by biopsy IHC markers like Pan-cytokeratin, P63, Synaptophysin, Chromogranin and TTF-1 were done in 47 cases to confirm the final diagnosis.

So in nutshell, out of 103 cases of lung malignancies, after IHC, 57 cases were proved to be squamous cell carcinomas, 21 cases as small cell carcinomas, 15 cases as adenocarcinomas, 4 cases as adenosquamous carcinomas, 3 cases as large cell neuroendocrine carcinomas, 2 cases as NET-Grade-2 and 1 case as NHL.

In conclusion squamous cell carcinoma is the most common histological type of lung cancer as is seen in this study also followed by Small cell carcinoma in this study which is comparable with the studies done by Khan et al, (2006).[14] Adenocarcinoma constituted 14.56% cases, which is comparable to the above studies but is at variance to western literature where incidence of adenocarcinoma has surpassed squamous cell carcinoma.[20]

CONCLUSION

Thus, in the present study yield of diagnosis was highest with the bronchoscopic biopsies and in maximum number of cases with a sensitivity of 88.034% and specific histologic diagnosis was made by biopsies and IHC only. Sensitivity of BAL in this study was 43.69% and specificity was 57.14%. Sensitivity of TBNA in this study was 55.34% and specificity was 50.0%. Though BAL and TBNA were inferior to bronchial biopsy in diagnosing lung malignancies but these were effective for peripheral lung malignancies and when the patient was at risk of hemorrhage.

Thus, author can say that combining three modalities of investigations like Bronchoscopy, BAL and TBNA we can diagnose cases of carcinoma lung much effectively than using individual modalities there by increasing sensitivity and specificity.

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