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Diagnostic utility of Liquid-Based Cytology in the Diagnosis of Lung Cancer

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Abstract: ***Lung cancer is worldwide most common cause of cancer related death. A use of Liquid- Based Cytology (LBC) in non-gynae has been increasing. Aims: To assess the diagnostic utility of LBC in the diagnosis of lung cancer from the aspirated material either by endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) or CT guided trans thoracic needle aspiration (TTFNA) from lung mass. Methods and Material: This study was conducted at the Department of Pathology, tertiary hospital. Sixty - one malignant cases were included in our study and their respective cytology smear has been prepared by both techniques LBC and Conventional Smear (CS), considered histopathology as a gold standard for concordance of the diagnosis. Results: Number of malignant case were diagnosed by LBC 72.3% where by conventional method 60.66% which does indicated a there is no statistical significance between the two groups (P = 0.180) but still few cases diagnosed by LBC were higher than CS, due to improvement of adequacy in LBC (86.89%) as compared to CS (65.57%). Conclusions: We can conclude that LBC was superior to CS in the diagnosis of aspirated material from the lung mass because it improves the adequacy of samples, as it is depend on automation technique.***

Keywords: Lung mass, Histopathology, Liquid based cytology, Conventional smear

1. Introduction

Lung cancer is also included in a worldwide most common cause of cancer related death in adult patients because of late presentation of symptoms and sign such as dyspnoea, cough, chest pain, hoarseness of voice and hemoptysis[1], [2]. Broad histological classification of lung cancers are Non-Small Cell Lung Cancer (NSCLC) and Small Cell Lung Cancer (SCLC), whereas NSCLC being more common [3], [4]. Adenocarcinoma, squamous cell carcinoma and large cell carcinoma are a further major subtype of NSCLCs.

Since early diagnosis of lung cancer by combining various method reduced the burden of death due to Lung cancer.Material obtained from lung mass either exfoliating cytology or aspiration cytology. Aspiration method {Endobronchial Ultrasound Guided Transbronchial Needle Aspiration (EBUS-TBNA) Or CT guided Transthoracic Fine Needle Aspiration (TTFNA)} has proved to be a quick, effective, physically non-traumatic, non-invasive and inexpensive method and provides us better yieldif correlated with clinical history and CT or MRI scan to localize the mass lesions [5]. EBUS-TBNA or TTFNA as an alternate to open biopsies is used for making definitive diagnosis but histopathological examination (HPE) remains the gold standard for diagnosis.

LBC has been well established for gynecological specimen [ThinPrep(TP) approved at 1996 & SurePath(SP) approved at 1999] but LBC uses is increasing in the non-gynaecological specimen as well, either by TP or by SP methods [6] - [10]. ThinPrep based on filtration method where preservative used is CytoLyst, while SurePath based on centrifugation method and the preservative used is CytoRich [11].CytoRich Blue is an alcohol-based fixative including ethanol and methanol and CytoRich Red is a formalin – based fixative including isopropanol, ethylene glycol, methanol, and formalin[12].

LBC technique improves the yield of diagnosis by providing uniform monolayer thick smear, less obscuring background by an elimination of obscuring blood and inflammatory exudate and removal of the air-drying artifact in a comparison to conventional smear [13], [14]. Left suspended material can be used for other ancillary tests like immunocytochemistry (ICC) and molecular biological tests.

2. Material and Methods

This present study was undertaken to assess the diagnostic utility of Liquid based cytology (LBC) in the diagnosis of lung cancer from the aspirated material either by EBUS-TBNA or CT guided TTFNA from lung mass.

This study was conducted in tertiary care hospital at the Department of Pathology, Study period was one year (August 2014- August 2015). After obtaining the complete clinical history, radiologic details and explaining the FNAC procedure and discussing the possible side effects, informed consent was obtained. Depend on site of a lesion they were subjected eitherto EBUS-TBNA or CT guided TTFNA.

In EBUS-TBNA, anesthetized site for aspiration, and aspiration was done by Olympus bronchoscope where 22 G needle used after localization of the mass lesion. While in CT guided TTFNA, aspiration site was made aseptic by using providone iodine. Local anesthesia was administered. A physician aspirated all the lesions, at least 2-3 passes and adequate sample were collected and conventional smears were made and fixed in 95% alcohol for Haematoxylin and Eosin (H&E) staining. Another prick was done to obtain fresh material for LBC procedure. Both sample were taken to cytology lab of pathology department for further process.

At cytology lab, conventional procedures include Haematoxylin and Eosin (H&E) staining while LBC technique includes SurePath. The conventional and LBC smears were examined independently by two pathologists unaware of their individual findings. The Cytohistological correlation was made. Histopathology was considered as gold standard for final diagnosis in all cases.

3. Results

Sixty-one patients suspected of lung cancer were included in the study where their respective histopathology reports were available for cytohistological corelation.

In the present study total number of malignant cases was 61, out of which nonsmall cell lung cancer was 90.1% and small cell lung cancer was 6.5%. (Table1).

Table 1: Histological diagnosis of observed studied

Number of Malignant cases (61)	Number of HPE Diagnosed specimens	Percentage
1- Non Small Cell Lung Cancer (NSCLC)	55	90.1
a) Adenocarcinoma	34	61.8
b) Squamous cell carcinoma	15	27.
c) Adenosquamous carcinoma	05	9.0
2-Poorly differentiated Epithelial	01	1.8
malignancy		
3- Small Cell Lung Cancer (SCLC)	04	6.5
4. Other tumor: a) Germ cell tumor	01	1.6
b) Carcinoid	01	1.6

Concordance of histopathology report with the LBC was comparable higher than Conventional Method but there was statically insignificant observed in the diagnostic concordance of malignant lesions by these two methods. (Table 2).

Table 2: Diagnostic Concordance LBC Versus CS of Malignant cases:

Histological Diagnosis	Total	Conventional		LBC		Statistical significance	
		No.	**%**	**No.**	**%**	**χ^2**	**P**
Malignant	61	37	60.66	44	72.13	1.800	0.180

Diagnostic efficacy of LBC is much higher in Squamous cell carcinoma than the adenocarcinoma. Whereas diagnostic efficacy was zero in another carcinoma, which included Poorly differentiated epithelial lung cancer, germ cell tumor and carcinoid cancer (Table 3).

Table 3: Diagnostic Efficacy of Cytological techniques

Histological Diagnosis	Total No.of cases diagnosed by HPE	No. of cases diagnosed by Conventional		No. of cases diagnosed by LBC		Statistical significance	
		No.	%	No.	%	χ^2	P
Adeno carcinoma	34	24	70.59	25	73.53	0.073	0.787
Squamous cell carcinoma	15	7	46.67	11	73.33	2.222	0.136
Adeno squamous carcinoma	5	4	80.00	5	100.00	1.111	0.292
Small cell carcinoma	4	2	50.00	3	75.00	0.533	0.465
Other carcinoma	3	0	0.00	0	0.00	0.000	1.000

Adequacy of LBC method was significantly higher as compared to the Conventional method in malignant case (p=0.006) (Table 4).

Table 4: Comparison of Adequacy of Malignant Lesions by Conventional & LBC Method

Cytological Preparation methods	Malignant (n=61)	
	No.	%
Conventional method	40	65.57
LBC	53	86.89
Statistical significance	χ^2=7.645; p=0.006	

4. Discussion

LBC uses in the non-gynaecological specimen have been increasing to improve the diagnostic yield of the specimen. This study was based on using of SP method in the diagnosis of Lung Cancer, where the aspirated material used and it obtained either by EBUS-TBNA or by CT-guided TTFNA.

Sixty-one cases with well-known histopathology as malignant cases were included in our study. FNA was carried out samples and taken in their respective preservative such as 95% alcohol for CS and CytoRich red for LBC. Further processed at the department of cytopathology lab of pathology department and smears were prepared, for conventional smears (2-4 slides) and LBC (1 slide) were prepared.

Of the histopathologically diagnosed cases; among malignant cases, NSCLC (90.1%) was more frequent histological type as compared to SCLC (6.5%)[15]. Among NSCLC, the percentage of adenocarcinoma was highest 34/55 (61.8%). On compilation of data lung cancer, by Behera and Balamugesh showed that various workers in India had reported the prevalence of adenocarcinoma lung between 3.6-34.3% and that of SCC between 25.7-73.3%. [16]

In our study, diagnosis by LBC was found to be concordant with the histology diagnosis in 72.13% malignant cases while concordance of conventional smear was 60.6%. Wallace et al reported the use of liquid-based-thin-layer cytology for Endobronchial ultrasound-guided lymph node aspiration as a method of diagnosing and staging lung cancer[SEP] and found that the use of liquid-based-thin-layer cytological techniques provides high-quality specimens for diagnostic purposes[17]. Concordance between the LBC and

conventional with respect to histology in the diagnosis of adenocarcinoma [Fig 1] was almost equal (73.3% by LBC and 70.6% by CS) but concordance between LBC and histology was more in the case of Squamous cell carcinoma [Fig 2] as compared to CS (73.33% by LBC versus 46.67% by conventional method).

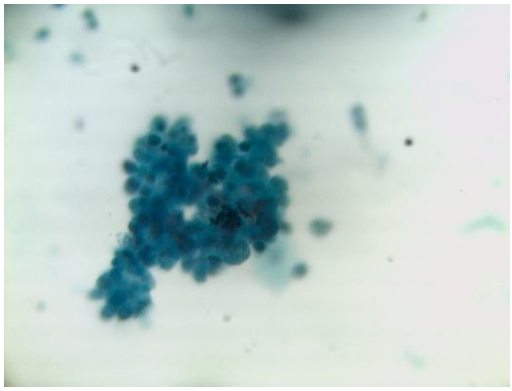

Figure 1: Liquid Based Cytology smear shows adenocarcinoma of lung x 200

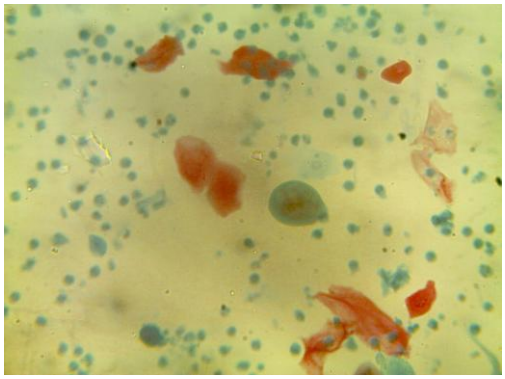

Figure 2: Liquid Based Cytology smear shows squamous cell carcinoma of lung x 200.

In the cases of germ cell tumor, carcinoid, and poorly differentiated epithelial malignancy smears were inadequate by both techniques. It may be due to failure to obtain material from the representative site. Specificity of both methods in the present study was 100%.

A number of cases diagnosed by LBC method were quite higher than the conventional method because adequacy rate were improved by the LBC method (86.89%) as comparison to the CS (65.57%).

In our study, we observed some advantages in LBC over CS. It was less time consuming as per interpretation with smaller screening area (13 mm) with a clear background since decreasing the number of the slide for diagnosis and possibility of adjunctive investigations like immunocytochemistry on the same material. Our study supports the view of Kobayashi et al. who found that TP preparations are superior to CP with regard to clear background, monolayer cell preparation and cell preservation [18]. However, TP preparations are more expensive than CP and require some experience for interpretation.

There are some disadvantages of LBC; background of smears important in making diagnosis lost during processing for example in the diagnosis of small cell carcinoma where diagnostic hints such as smearing and molding are less pronounced in SP However, the cellular features are well preserved hence the specificity is comparable [19].

Though LBC offers an advantage of cell - block preparation from left over material for further ancillary techniques but procedures like flow cytometry cannot be performed which requires unfixed cellular material.

Number of cases diagnosed by LBC was quite higher than the CS in Lung mass lesion. All over LBC smears yielded better cellularity and preserved morphological features. The diagnostic sensitivity of LBC was better than CS. Moreover, there is always a learning curve in LBP interpretation and training is needed before someone starts interpreting these preparations because of fine alterations of morphology and cellular size.

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