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A Study on Accuracy of Respiratory Cytology for Cancer Diagnosis

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Abstract: ***Sputum cytology has been the traditional focus for teaching respiratory cytology for many years. However emphasis has been altered by the introduction of Fibreoptic brochoscopy and Fine needle aspiration. Bronchial brushings, washings, fine needle aspiration and lavage procedures usually yield better diagnostic material than that is obtained by simple exfoliative sampling. The combined use of cytology and biopsy facilitates accurate classification of tumour type and enhances sensitivity of diagnosis of malignant tumours. Aim: To evaluate our Institutional experience with bronchial washings, brush cytology and biopsy as diagnostic tools to enhance the sensitivity of malignant tumours. Methodology: Bronchial washings, brushings and biopsy were obtained by using Fibreoptic bronchoscope from 40 patients. The cytology samples were received as unstained smears. The slides were stained with standard H&E stains. The biopsy specimens were fixed in neutral buffered formaldehyde, processed to paraffin blocks and also stained with H&E stains. Observation and Results: Among the 40 cases studied, 17 were Squamous cell carcinoma, 3 were small cell carcinoma, 2 were adenocarcinoma. 22 were diagnosed to be 'positive for malignancy' by cytology as well as biopsy. Conclusion: The accuracy of bronchial cytology is high enough to warrant its use in combination with bronchial biopsy in the diagnosis of lung cancer. Our study shows that a combination of three diagnostic modalities - bronchial washings, brushings and biopsy is the best strategy in the diagnosis of bronchoscopically visible lung cancer.***

Keywords: Fibreoptic bronchoscopy, Bronchial brushing, Bronchial washing, Bronchial biopsy, Lung cancer

1. Introduction

Sputum cytology has been the traditional focus for teaching respiratory cytology for many years. However emphasis has been altered by the introduction of Fibreoptic brochoscopy and Fine needle aspiration [25]. Recent developments in sampling techniques have changed the practice of respiratory tract cytology, although new methods have not completely supplanted more traditional ones. Methods for obtaining cell samples from respiratory tract include sputum bronchial brushing, bronchial washing, bronchioalveolar lavage, transbronchial needle aspiration, transthoracic fine needle aspiration and endoscopic ultrasonography guided fine needle aspiration. Each of these methods has advantages and limitations. Bronchial brushings, washings, fine needle aspiration and lavage procedures usually yield better diagnostic material than that is obtained by simple exfoliative sampling [25].

Bronchial washing is complementary to brushing when a endobronchial lesion is observed and superior to brushing when the lesion is beyond the reach of the brush. It is also helpful in the diagnosis of peripheral lung lesions with submucosal or peribronchial tumour spread [21]. Washings are sent as part of the procedure and are routinely processed and add a small increment to sensitivity, mainly when brush or biopsy cannot reach more peripheral tumours [25].

Bronchoalveolar lavage is another technique particularly useful when a diffuse infilterate is seen on the X-ray and an opportunistic infection or lymphangitic spread of tumour is suspected. The bronchoalveolar lavage may provide a higher yield than bronchial washing for diagnosis of peripheral tumours particularly adenocarcinoma and bronchioalveolar carcinoma.

A combination of cytologic modalities is often performed with or without forceps biopsy to increase the diagnostic yield [21]. While forceps biopsy is suitable for endobronchial mass lesions, bronchial brushing allows sampling of a larger mucosal area.

A combined study of cytology and biopsy material enhance the sensitivity of diagnosis of malignant tumours and their specific subtyping. The combined use of cytology and biopsy facilitates accurate classification of the tumour type, since cytologic samples often provide better morphologic preservation the cells and lower likelihood of crushing artifacts, whereas histologic samples better demonstrate tissue architecture and provide more material ancillary techniques such as immunohistochemistry. Thus, even in the presence of an endobronchial lesion, collection of cytologic samples is recommended in addition to forceps biopsy.

2. Review of Literature

Respiratory cytodiagnosis had its birth in the late 1800s. George N. Papanicolou and Koprowska were the first to report the cytological findings from the case of carcinoma in situ of the lung [25]. The development of the rigid bronchoscope in the late 19th century by Gustav Killian, formed the foundation of a technology by which the mucosal surface of the bronchi could be directly visualised and sampled for both tissue and cellular evaluation. Dr. S. Ikeda

was the inventor of the Olympus Flexible Fiberoptic Bronchoscope [5].

Most authors agree that the accuracy of lung cancer diagnosis is greatly improved multiple sampling methods are employed [21]. On average, each cytological method detects about one – half to two-thirds of the lung cancers. Combining multiple methods results in a sensitivity of about 80% i.e. is equal to higher than that of bronchial forceps biopsy. Biopsy and cytology are complimentary, however by using both methods a detection rate as high as 85% to 90% can be achieved [21].

In an extensive study of the results of pulmonary cytology emanating from the laboratory of Koss, L.G., (*Koss et al,* 1964), it was emphasized that careful collection and processing of material were essential in order to achieve satisfactory diagnostic results [16].

Bronchial aspirates and washings: Introduction of the bronchoscope in the lower respiratory tract enables the examiner to obtain specimens by means of a suction apparatus that aspirates secretions. Washings from the visualized areas may also be collected by instilling 3-5ml of a balanced salt solution through the bronchoscope and re-aspiration of the resulting material. Once the bronchoscope is removed direct smears may be made with immediate fixation in 95% ethyl alcohol. Bronchial wash has a lower diagnostic yield than Bronchial brushing. However it is important for diagnosis of peripheral lesions, infections and bronchioalveolar carcinoma [5].

Bronchial brushing: By using flexible fiberoptic bronchoscope it is possible to visualise and brush a suspected lesion and submit the resulting cytologic material for laboratory examination [5]. The Bronchial brushing and washing is safe, rapid, cost-effective and gives a higher rate of sensitivity and accuracy[2].

Recent technologic advances in Bronchoscopy continue to improve our ability to perform minimally invasive, accurate evaluations of the tracheobronchial tree and to perform an ever increasing array of diagnostic, therapeutic and palliative interventions [11].

It is equally important that the respirologist, interventional radiologist, and thoracic surgeon understand the importance of obtaining a satisfactory amount of material, because the specimens obtained ultimately affect the patient's management and prognosis [9].

3. Aims and Objectives

The present study is designed to emphasize the diagnostic effectiveness of conventional respiratory cytologic methods and to advocate the combined use of fibreoptic bronchoscopy in order to complement the cytologic diagnosis of lung cancer.

4. Material and Methods

40 samples of Bronchial washings, brushings and biopsy were obtained from patients with the help Flexible Fiberoptic Bronchoscope in the Department of Thoracic medicine at Govt. Vellore Medical College, from Jan 2015 to Dec 2016 and studied. There was no age restriction. The age of the patients ranged from 20 to 80 years. Of these 40 cases, 29 were males and 11 were females. The bronchial washings, brushing and biopsy samples were received at our lab in the Department of Pathology. The cytology smears were stained standard H & E stain. The biopsy specimens were fixed in Neutral buffered formaldehyde, processed to paraffin blocks and also stained with H & E stain.

5. Observation and Results

Accuracy is to a great extent influenced by the expertise of the aspirator and the pathologist as well as the methodology used to prepare the sample in the laboratory. In total of 40 cases studied, 22 cases were diagnosed as 'positive for malignancy' by cytology as well as biopsy of which 17 were Squamous cell carcinoma, 3 were small cell carcinoma, 2 were adenocarcinoma. In our study of patients diagnosed as malignancy, majority (35.3%) were in the age group of 51 – 60 years.

I. No. of True positive cases – 22
II. No. of True negative cases – 12
III. No. of False negative cases – 05
IV. No. of False positive cases – 01

Table 1:

Bronchial cytology	Bronchial Biopsy (HPE)		Total
	Positive cases	Negative cases	
Positive	22	01	23
Negative	05	12	17
Total	27	13	40

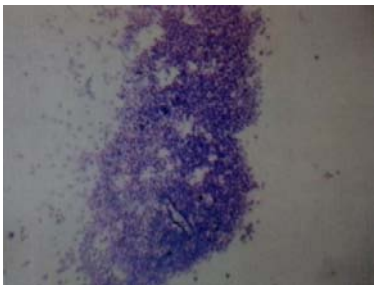

Figure 1: Cytology - Smear positive for malignancy – Small cell carcinoma

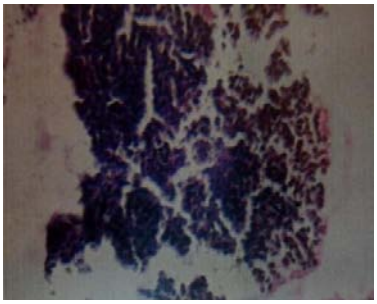

Figure 2: HPE -Small cell carcinoma (H&E stain x 400x)

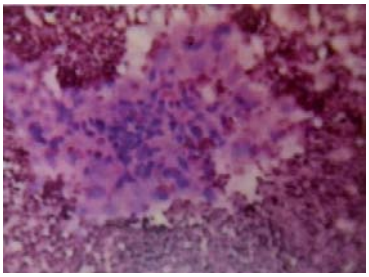

Figure 3: Cytology - Smear positive for malignancy (H&E stain x 400x)

6. Discussion

The sensitivity, specificity, accuracy, positive and negative predictive value of brush cytology were calculated relative to the final histopathologic status as follows:

Sensitivity [22] = $\frac{TP}{TP + FN}$

Specificity [22] = $\frac{TN}{TN + FP}$

Accuracy [22] = $\frac{TP + TN}{TP + FP + FN + TN}$

Positive Predictive Value [22] = $\frac{TP}{TP + FP}$

Negative Predictive Value [22] = $\frac{TN}{TN + FN}$

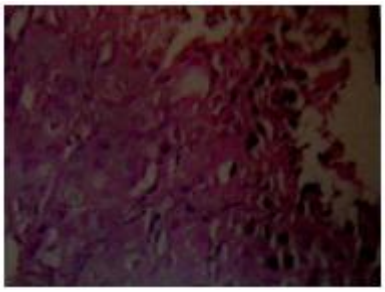

Figure 4: HPE –Moderately differentiated Squamous cell carcinoma (H&E stain x 400x)

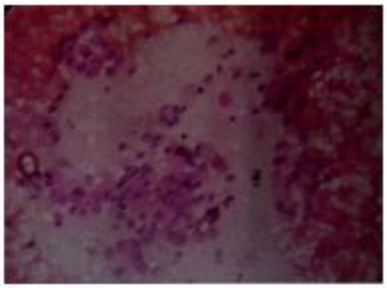

Figure 5: Cytology - Smear positive for malignancy – Adenocarcinoma (H&E stain x 400x)

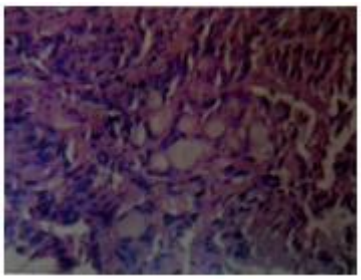

Figure 6: HPE - Adenocarcinoma (H&E stain x 400x)

Table 2:

A.	*Sensitivity*	81.48%
B.	*Specificity*	92.30%
C.	*Positive Predictive Value*	95.65%
D.	*Negative Predictive Value*	70.58%
E.	*Accuracy*	85%

The sensitivity and specificity are important factors in deciding the accuracy of the diagnostic test. The sensitivity of bronchial cytology in our study is 81.48% whereas in other studies it ranges from 38 to 96%. The number of negative cases was 5. False negative diagnosis is usually a result of sampling error and rarely due to interpretation error.The accuracy of the test in this study is 85% which is the reference range of the most widely acclaimed studies published earlier.

Table 3

Investigator	*Year*	*Specimen type*	*Sensitivity (%)*	*Specificity (%)*
Erosan and Frost	1970	Bronchial washing	61	Not Supplied
Bibbo *et al*	1973	Bronchial brushing	70	98
Bedrossian *et al*	1976	Bronchial washing Bronchial brushing	76 76	Not Supplied
Johnston and Bossen	1981	Bronchial washing Bronchial brushing	22 87	99.9
Pilotti *et al*	1982	Bronchial brushing	67	Not Supplied
Ng and Horak	1983	Bronchial washing	74	Not Supplied
Truong *et al*	1985	Bronchial washing Bronchial brushing	66 77	99.9
Anupam Sarma *et al*	2013	Bronchial washing Bronchial brushing Bronchial biopsy	89.96	90.9
Present Study	2016	Bronchial washing Bronchial brushing Bronchial biopsy	81.48	92.3

7. Conclusion

Our study suggests that the accuracy of bronchial cytology (brushing and washing) is high enough to warrant its use in combination with bronchial biopsy in the diagnosis of lung cancer [5]. The correlation between cytologic and histologic diagnosis is excellent in well differentiated squamous cell carcinoma, small cell carcinoma and adenocarcinoma, but lower for other poorly differentiated tumours, because of the overlap of cytomorphologic features of these neoplasms. A combination of cytomorphology and immunocytochemical stains is highly effective in

differentiating primary lung carcinomas from metastatic neoplasms.

From the results of our study, we conclude that pulmonary cytologic techniques have excellent sensitivity and accuracy in the diagnosis of lung carcinomas. Hence we recommend that a combination of the three diagnostic modalities – bronchial washing, brushing and forceps biopsy is the best strategy in the diagnosis of brochoscopically visible lung cancer.

8. Future Scope

All the ancillary studies that are performed on tissue samples, (histochemical stains, immunocytochemical studies, flow cytometry and molecular tests) can also be done on cytology samples to compliment the cytological diagnosis of lung cancer.

References

[1] Accard JL, Marsan C, Babo P, Cana E, Thenault D : Brushings and bronchial biopsies in small cell cancer-comparison of results. Rev.Mal.Respir.1985: 2(3): 127-32
[2] Anupam Sarma J. D. Sharma, C. Bhuyan, A. C. Kataki, R. A. Sangma: A Study of Cytological Evaluation of Bronchial Washing and Brushing in Bronchogenic Carcinoma. International Journal of Scientific and Research Publications 2013 : 3(8) ; 1-7
[3] Barbara F. Atkinson – Atlas of Diagnostic cytopathology, 2nd edition, 2004.
[4] Bejni- Thivolet F, Guerin JC: Cytologic examinations during bronchial endoscopy, bronchial brushing and aspiration Rev.Mal.Respir.1992: 9(1): 23-30.
[5] Bibbo – Comprehensive cytopathology William W, Johnston, Craig E.Elson, Chapter 16, 2nd edition.
[6] Boucher CD, Yoneda K – Cytologic characterisation of bronchial epithelial changes in small cell carcinoma of lung. Acta.Cytol. 1995: Jan- Feb; 39(1):69-72.
[7] Fraire AE, McLarty JW, Greenberg SD. Changing utilisation of cytopathology versus histopathology in the diagnosis of lung cancer. Diagn. Cytopathol. 1991; 7(4): 359-62.
[8] Fuladi AB, Munje PR, Tayade BO. Value of Washings, Brushings and Biopsy at Fibreoptic Bronchoscopy, JCACM 2004: 5(2): 137-42
[9] Gahlot A, Mogra N. Role of Fiberoptic Bronchoscopy in Histopathological Analysis of Lung Lesions. IAIM, 2016; 3(4): 130-135.
[10] Goel MM, Sanjay Uprati, Rajendra Prasad. Observer perception variability in Bronchial Brush cytology 16(2): 75-83, 1999.
[11] Herth F.J.F. Bronchoscopic techniques in diagnosis and staging of lung cancer; Breathe 2011 7: 324-337
[12] Jay SJ, Wehr K, Nicholson DP, Smith AL. Diagnostic sensitivity and specificity of Pulmonary cytology. Acta. Cytol. 1980. Jul-Aug 24(4): 304-312.
[13] John D. Bancroft, Marilyn Gamble. Theory and practice of histological techniques, 5th edition, 2002.
[14] Jones AM, Hanson IM, Armstrong GR et al. Value and accuracy of cytology in addition to histology in the diagnosis of lung cancers at flexible bronchoscopy. Respiratory Medicine – 2001: 95(5): 374-8.
[15] Lam WK, So SY, Hsu C, Yu DY. Fibreoptic Bronchoscopy in the diagnosis of Bronchial cancer – comparison of washings, brushings and biopsies in central and peripheral tumours. Clin. Oncol, 1983; Mar.9(1): 35-42.
[16] Leopold G. Koss- Diagnostic cytology and its Histopathologic bases 3rd edition, 1979.
[17] Mak VH, Johnston ID, Hetzel MR, Grubb C. Value of washings and brushings at flexible bronchoscopy in the diagnosis of lung cancer. Thoracic 1990, May $%(5): 373-6.
[18] Millerom B,Broquie G, Castelain G, Solignee P, Brocard H, Cytological diagnosis of bronchial cancer from samples obtained by broncho-fibroscopy. Sem.Hop.1977; Jul 10-20; 53(25-28)
[19] Payne CR, Hadfield JW, Stivin PG, Barker V, Heard BE, Stark JE. Diagnostic accuracy of cytology and biopsy in primary bronchial carcinoma. J.Clin.Pathol. 1981; Jul 34(7): 773-8.
[20] Saita S, Tanzillo A, Riscica C, Maresca A, Potenza E, D'Arrizo M. Bronchial brushing and biopsy a comparative evaluation in diagnosing visible bronchial lesions. Eur.J.Cardiothoracic Surg.1990; 4(5):270-2
[21] Silverberg's Principles and Practice of Surgical and Cytopathology. 4th edition, 2006, Vol.I – Ch -18.
[22] Speicher C, Smith JW Jr. Choosing Effective Laboratory Tests, WB Saunders, 1983.
[23] Speider P, Joder P, Bronchial cytology –value of various methods for the diagnosis of primary lung neoplasms. Schwiz. Med Wochenschr. 1979; Jun 2; 109(22): 834-7.
[24] Troung LD, Underwood RD, Greenberg SD, McLarty JW, Diagnosis and typing of lung carcinoma by cytopathologic methods. Acta. Cytol 1985, May-Jun; 29(3) : 379-84.
[25] Winfred Gray – Diagnostic cytopathology, 1995.

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