Original article

Efficacy of Bronchoalveolar Lavage In Diagnosing Lung Malignancy

Sharma Khilanath[1*], Sharma Chandra Prasad[2]

[1]Department of Pathology, [2] Department of Respiratory Medicine and Critical Care, Nivedita Multi speciality Hospital, Pradhan Nagar, Siliguri.

ABSTRACT

Background: Due to new therapeutic options in thoracic oncology, the pathological diagnosis of bronchial carcinoma has become more challenging. The majority of bronchial cancer is diagnosed from small biopsy specimens and the diagnosis are often based on cytological methods. **Aims:** In this study, we evaluated bronchoalveolar lavage specimens of 333 patients in order to determine the diagnostic reliability of bronchoalveolar lavage cytology by correlating them with bronchial biopsies performed in our hospital. **Material and methods:** In our center, bronchial lavage/bronchoalveolar lavage (BL/BAL) specimens are obtained and subsequently processed. Sensitivity, specificity, as well as accuracy of cytological tumor typing were determined using histopathology of tissue biopsy (TB) as gold standard. **Results:** Three hundred and thirty three BAL samples were studied. Forty six cases were available for bronchial biopsy comparison, out of which forty two were malignant and four were benign lesions. The sensitivity and specificity of cytology were 88.57% and 90.90%, respectively. Sub classification of lung carcinoma into small cell carcinoma, squamous cell carcinoma and adenocarcinoma was possible in 100%, 88.8% and 76.4% cases respectively. **Conclusions:** Cytology is a reliable diagnostic tool in the diagnosis of lung malignancies. Subsequent sub classification of the tumour by cytology was possible in more than 88% of cases.

KEYWORDS: Bronchoalveolar Lavage, Cytology, Malignancy.

INTRODUCTION

Bronchoalveolar lavage (BAL) explores large areas of the alveolar compartment providing cells as well as non-cellular constituents from the lower respiratory tract. It opens a window to the lung. Alterations in BAL fluid and cells reflect pathological changes in the lung parenchyma. With the introduction of flexible fiber-optic bronchoscope around 1970, various bronchopulmonary lesions, otherwise unreachable with rigid body bronchoscope, became more easily accessible [1]. With this instrument the techniques like bronchial brushings (BB), BAL) and transbronchial needle aspiration (TBNA) became popular tools for obtaining diagnostic cytological material from various sites of the tracheo-bronchial passage [2].

Today, these cytological procedures constitute the most useful and least expensive investigative tools available for the detection of pulmonary diseases, especially lung cancer. Respiratory tract cytology is well established throughout the world as a vital diagnostic procedure in the evaluation of any patient with suspected lung malignancy. Our aim was to study and compare the efficacy of this very popular cytological technique in diagnosing carcinoma of lung by correlating them with histopathological diagnosis by bronchial biopsy.

MATERIALS AND METHODS

The study was conducted at a tertiary care hospital, in Eastern India. From 1st June 2013 until 30th March 2015, a total of 333 BAL specimens from tracheo-bronchial lesions were collected. The samples were obtained by flexible fiber-optic bronchoscopy done by the pulmonologist. BAL samples were received as 20ml aliquots of normal saline in sterile vials. Samples were centrifuged and prepared into air-dried and wet-fixed smears. The air dried smears were stained with May-Grunewald Geimsa and the wet fixed slides with Papanicolaou and Hematoxylin & Eosin stains. Bronchial biopsies were received in 10% formalin.

Statistical Analysis

All data were analyzed using the Statistical Program for the Social Science version 17.0 (SPSS Inc., Chicago, Illinois). Computed statistics included medians and ranges for continuous variables, and frequencies and percentage frequencies for categorical variables. Sensitivity, specificity, positive predictive value and negative predictive value of bronchial cytology were calculated according to the literature [3].

RESULTS

In our study group (n=333), 42 cases (12.6%) were found to be positive for primary carcinomas of lung. Patient demographics was between 51-70 years old (38 males and 4 females), with the most number of cases between the ages 61-70 years of age [Table 1].

Table 1: Age and sex distribution of carcinomas on Bronchoalvedolar Lavage [N=42]

Age Group(Years)	Total	Male (%)	Female (%)
31 – 40	01	00	01(100%)
41 – 50	05	04(80%)	01(20%)
51 – 60	16	14 (87.5%)	02(12.5%)
61 – 70	15	15(100%)	00
71 – 80	05	05(100%)	00
81 – 90	00	00	00
Total	42	38(90.5%)	4(9.5%)

The study shows the spectrum of bronchopulmonary cytologic diagnoses with follow-up biopsies [n=42]. An overall male preponderance was seen, male to female ratio [9.5:1].Squamous cell carcinoma (SCC) had the largest morphological group [n=18/42, 42.8%;],followed by adenocarcinoma (AC) [n= 17/42.4%]. Cytologically, 2 cases [4.7%] could be categorized as poorly differentiated Non small cell carcinoma (NSCLC) [Table 2]. The study also shows the diagnostic positivity of BAL, in terms of true positive, true negative, false positive and false negative cases. Cases which did not have concurrent biopsies were not included in this study [Table 3].

Table 2: Distribution of carcinomas according to cytomorphology [n=42]

Cytomorphological Diagnosis	Total	Male(%)	Female(%)
Squamous Cell Carcinoma(SCC)	18	18(100%)	00
Adenocarcinoma(AC)	17	14(82.4%)	03(17.6%)
Small Cell Carcinoma (SCLC)	05	04(80%)	01(20%)
Poorly Differentiated Non small cell Carcinoma(NSCLC)	02	02(100%)	00
	42	38(90.5%)	04(9.5%)

Table 3: Diagnostic positivity of Bronchoalvedolar Lavage in carcinoma lung

Procedure	Total Cases	Case compared with biopsy	TP	TN	FP	FN
BAL	**333**	**46**	**31**	**10**	**1**	**4**

TP=True Positive, TN= True Negative, FP= False Positive, FN=False Negative

Assessment of Accuracy of Cytologic Tumor Typing

Cytologic typing of SCC, AC, and Small Cell Carcinoma (SCLC) was confirmed by histology in 72.2% (13/18), 82.3% (14/17) and 80% (4/5), respectively. In one case, biopsy was negative(a false positive by cytology).There were 4 [11.11%]false negative by cytology. 2/42 cases (4.76%) were cytologically diagnosed as NSCLC. By histology, these cases were subclassified as AC (1 case), and SCC (1 case). There were 10 true negative cases.

Table 4: Parameters of accuracy of Bronchoalvedolar Lavage in Neoplastic lesions of lung

S. No	Parameters	Results
1	Sensitivity	88.57%
2	Specificity	90.90%
3	False positivity	9.00%
4	False negativity	11.42%
5	Positive predictive Value	96.87%
6	Negative predictive Value	71.42%
7	Accuracy	89.13%

DISCUSSION

Lung cancer is the most common malignant disease worldwide. It is the leading cause of cancer deaths in developed countries and is also rising at alarming rates in developing countries [4, 5]. It accounts for 13 per cent of all new cancer cases and 19 per cent of cancer related deaths worldwide [6]. There were 1.8 million new lung cancer cases estimated to occur in 2012 [7]. In India, lung cancer constitutes 6.9 per cent of all new cancer cases and 9.3 per cent of all cancer related deaths in both sexes. Deaths due to lung cancer are more than those due to colorectal, breast and prostate cancers combined. It was considered to be rare in the beginning of the century but has now reached almost epidemic proportions. This is the single most devastating cause of cancer-related deaths with approximately 1.5 million cases world-wide and more than 1.3 million cancer-related deaths in 2001[8,9].

There is a great variation in the prevalence of lung cancer in different geographical areas. In India, the prevalence of lung cancers shows much variability from one region to other [10]. In the most recent study, It is the commonest cancer and cause of cancer related mortality in men, with the highest reported incidences from Mizoram in both males and females (Age adjusted rate 28.3 and 28.7 per 100,000 population in males and females, respectively) In a study published from Jammu, in 1993, lung was the most common site for malignancy [11]. Reports of National Cancer Registry Program of Indian Council of Medical Research, from Bhopal, Delhi and Mumbai, also show lung to be the top site for malignancy amongst males [12].

Lung cancer constituted 14.4% of all cancers in a review of 9210 consecutive autopsies by Banker et al [13]. Sirsat et al reported that lung cancer formed one per cent of all cancers in Tata Cancer Hospital [14]. Viswanathan *et al* collected information from different hospitals of the country and found that the incidence of lung cancer in a hospital population was 27.4 per million in 1950 and in 78.6 per million in 1959 [15]. They also found an increase in the incidence of bronchogenic carcinoma (16.1 in 1950 to 26.9 in 1961 per 1000 malignancies), following analysis of the records of 15 teaching institutions in India over a period of 10 years.

International comparison of incidence rates of lung cancer with that seen in India showed a low figure (age adjusted rates of 66.5-100.4 in Europe and USA *versus* 2.0 to 14.6 per 105 in India males; the same is 16.1 to 33.3 *vs* 0 to 3.7 in females). However because of the overall population size, the absolute number should be large.

Due to new developments in the field of oncology, the pathological diagnosis of bronchial carcinoma has become more challenging [16]. According to Travis et al. in daily practice more than 70% of clinically suspected lung cancers are diagnosed by means of small biopsies or cytology. They reported 10% - 30% NSCLC diagnosed by small biopsy and cytology samples [17]. In our department the rate of primary lung cancer diagnosed by lavage specimens in combination with small biopsies, such as BB and CT-guided FNAC is even higher (>95%).

BAL and BB are valuable tools in the diagnostic process of lung cancer, but in the literature low sensitivities of washing procedures are reported. With flexible bronchoscopy and BAL for central bronchogenic carcinoma the sensitivities range from 31% to 78% [17] Sensitivity of flexible bronchoscopy combined with BAL in peripheral lesion has been reported to range from 12% to 65% [18].

Annette Zimpfer et al reported 83.0% and 83.4 % sensitivity and specificity respectively for BAL in diagnosing lung malignancies [19]. Rennard SI found malignant cells in 69% of BAL specimens [20]. Troung et al. reported an overall sensitivity of bronchial washing of 66% [21]. In our study an overall sensitivity of 88.57.0% was calculated for both centrally and peripherally located lung tumors and thus ranks in the upper range of reported sensitivities. This might probably be due to the specific procedure performed in our departments, since two BAL specimens are obtained and evaluated in association with BB.

Some studies have shown that definitive diagnosis of malignancy was possible by cytology alone. Naryshkin et al., who examined the reliability of bronchoscopic cytology in relation to biopsy, found a rate of 10.7% of nondiagnostic biopsies because of peripheral location of the tumour [22]. V. H. Mak et al and A. M. Jones et al have demonstrated diagnostic rates of 9.5% and 2.1% for bronchial washing (without histological confirmation) respectively [23,24]. We identified 6/42 (8.0%) cases in which only cytology was diagnostic or generated an abnormal result leading to further investigation. In in four of these cases, a peripheral located

tumor was not visible and not accessible by BAL, leading to a false negative result.

As compared with TB, lavage cytology led to a very low rate of 1 false positive diagnosis in our study. In this case, an inflammatory condition was found on biopsy. Taking all of this into consideration, false positivity by cytology occurred in 1/42 (2.3%). In this case no unnecessary treatment was administered as the cytology reports were cautiously formulated, and the negative results of the histological examination were adjusted by interdisciplinary review with consideration of additional investigations (e.g. microbiology tests).On the other hand, there were 4 cases of negative BALs which yielded a positive tissue biopsy presumably due to inaccessibility of the peripherally located tumor by BAL.

Assessment of accuracy of cytological tumor typing was highest in SCLC (100%) followed by SCC (88.8%), and 76.4% for AC. As in the literature, the cytological typing of SCC and SCLC was accurate but was less satisfactory for the other types of primary lung carcinomas except AC. Difficulties in cytological tumor typing arose especially in poorly differentiated carcinomas. Other reasons were a low cell number (often seen in BAL/BL samples); bad material preservation and inflammatory background [25, 26, 27].

No Large cell carcinoma was diagnosed in our study. By cytology, 6 cases were classified as poorly differentiated Non small cell carcinoma. In biopsy, 4 were diagnosed as AC and 2 as SCC.

CONCLUSION

In our study, pulmonary cytopathological methods have excellent sensitivity and specificity in the diagnosis of primary lung carcinomas. Our study shows that the combination of BL/BAL and biopsy can establish the diagnosis of bronchial carcinoma in most cases and allows the sub classification of NSCLC in more than 88% of cases.

REFERENCES

1. Ng ABP, Horak GC. Factors significant in the diagnostic accuracy of lung cytology in bronchial washing and sputum samples. ActaCytol1983; 27: 397-402.

2. Reynolds HY. Bronchoalveolar lavage.Am Rev Respir Dis 1987;135 : 250-63.

3.H. Motulsky, Intuitive Biostatistics, Oxford University Press, Oxford, 1995.[Citation   Time(s):1]

4. Husain AN, Kumar V. The lung. In: Kumar V, Abbas AK, FaustoN, editors. Robbins and Cotran pathologic basis of disease. 7th ed. India: Saunders; 2004. p. 711-72.

5. Cersosimo RJ. Lung cancer: a review. Am J Health Syst Pharm2002; 59 : 611-42

6. Malik PS, Raina V. Lung cancer: Prevalent trends & emerging concepts. Indian J Med Res 2015;141:5-7

7. J. Ferlay, I. Soerjomataram, R. Dikshit, S. Eser, C. Mathers, M. Rebelo, D.M. Parkin, D. Forman, F. Bray (2014). Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. International Journal of Cancer doi:10.1002/ijc.29210 PMID:25220842 Published online 9 October 2014.

8. Parkin DM, Muir CS. Cancer incidence in fivecontinents : Comparability and quality of data.IARC Sci Publ1992; 120 : 45-173.

9. Khuri FR, Herbst RS, Fossella FV. Emergingtherapies in non-small cell lung cancer.AnnOncol2001;12 : 739-44.

10. D. Behera, T. Balamugesh: Lung cancer in India: Review article. Indian J Chest Dis Allied Sci 2004; 46: 269-281

11. Kapoor R, Goswami KC, Kapoor B, Dubey VK. Pattern of cancer in Jammu region (Hospital based study 1978- 87). Indian JCancer 1993;30: 67-71.

12. Annual Report 1982: National cancer registry. Indian council of medical research, New Delhi, 1985. http://www.ncrpindia.org/Annual_Reports.aspx

13. Banker DD. J Post Grad Med 1955; 1 : 108.(Quoted in Nagrath SP, Hazra DK, Lahiri B, Kishore B, Kumar R. Primary carcinoma of the lung: Clinicopathological study of 35 cases. Indian J Chest Dis 1970; 12 : 15-24.

14. Sirsat MV. Some aspects of the pathology of primary carcinoma of the lung.J Postgrad Med 1958;4: 6-14.

15. Viswanathan R, Gupta S, Iyer PVK. Incidence of primary lung cancer in India.Thorax 1962; 17: 73-76.

16. K. M. Kerr, Pulmonary Adenocarcinomas: Classification and Reporting, Histopathology 2009; 54:12-27.

17. W. D. Travis, E. Brambilla, M. Noguchi, et al., International Association for the Study of Lung Cancer/ American Thoracic Society/European Respiratory Society International Multidisciplinary Classification of Lung Adenocarcinoma, Journal of Thoracic Oncology 2011; 6: 244-285.

18. G. Schreiber and D. C. McCrory, Performance Characteristics of Different Modalities for Diagnosis of Suspected Lung Cancer: Summary of Published Evidence, Chest 2003; 123: 115-128.

19. Annette Zimpfer1, Antonia Polak, Andrea Bier,et al. Assessment of Diagnostic Accuracy of Bronchoalveolar Lavage Cytology in the Diagnosis of Lung Tumors and Contribution to the Classification of Non-Small Cell Lung Cancer Entities: A Retrospective Clinocopathological Study. Open Journal of Pathology 2013; 3: 107-112

20. S. I. Rennard, Bronchoalveolar Lavage in the Diagnosis of Cancer, Lung 1990; 168(Suppl.1):1035-1040.

21. L. D. Truong, R. D. Underwood, S. D. Greenberg and J. W. McLarty, Diagnosis and Typing of Lung Carcinomas by

Cytopathologic Methods. A Review of 108 Cases, ActaCytol 1985; 29: 379-384.

22. S. Naryshkin, J. Daniels and N. A. Young, Diagnostic Correlation of FiberopticBronchoscopic Biopsy and Bronchoscopic Cytology Performed Simultaneously, Diagnostic Cytopathology 1992; 8: 119-123

23.V. H. Mak, I. D. Johnston, M. R. Hetzel and C. Grubb, Value of Washings and Brushings at Fibreoptic Bronchoscopy in the Diagnosis of Lung Cancer, Thorax 1990; 45:373-376.

24.A. M. Jones, I. M. Hanson, G. R. Armstrong and B. R. O'Driscoll, Value and Accuracy of Cytology in Addition to Histology in the Diagnosis of Lung Cancer at Flexible Bronchoscopy, Respiratory Medicine2001; 95: 374-378

25. J. P. Crapanzano and A. Saqi, Pitfalls in Pulmonary Cytopathology, Diagnostic Cytopathology 2011; 39: 144-154.

26. R. S. Saad and J. F. Silverman, Respiratory Cytology: Differential Diagnosis and Pitfalls, Diagnostic Cytopathology 2010; 38: 297-307.

27. L. Policarpio-Nicolas and M. R. Wick, False-Positive Interpretations in Respiratory Cyto-Pathology: Exemplary Cases and Literature Review, Diagnostic Cytopathology 2008; 36: 13-19.

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*Corresponding author: Dr Khilanath Sharma
E-Mail:khila23@gmail.com