ABSTRACT

Sputum cytology is a simple, accurate, reliable, cost effective and non-invasive procedure for the diagnosis of pulmonary lesions including preinvasive and invasive malignancies. BAL (Bronchoalveolar lavage) is a valuable diagnostic and research tool in pulmonology.

Aims: To compare the efficacy of Sputum cytology with BAL in the diagnosis of lung cancer.

Material and Methods: 2 year study was carried out. Sputum cytology, BAL and bronchoscopic biopsies were done in 97 cases. Comparison of effectiveness of Sputum cytology and BAL in diagnosing lung cancer is done with 'z' test.

Results: Total 97 cases were included in the study, 33 cases were positive for malignancy. Sensitivity of sputum cytology and BAL were 30% and 69.6% respectively. On applying ‘z’ test for statistical analysis p value of <0.0001 is obtained. Hence we conclude that there is a significant difference in proportions between sputum cytology and BAL in diagnosing lung cancer. So BAL is more effective diagnostic modality for lung cancer in comparison to sputum cytology.

Conclusion: BAL cytology is significantly more effective in the diagnosis of lung cancer in comparison to sputum cytology. As sputum cytology is a simple, reliable, cost effective and non-invasive procedure it can still be used as one of the diagnostic modality for lung cancer with fairly good sensitivity.

INTRODUCTION

Sputum cytology is an example of exfoliative cytology, which is based on the exfoliation of cells from the lining of the organ into a cavity from which cells can be obtained by a non-invasive means. (Myron et al., 2009) It is a simple, accurate, reliable, cost effective and non-invasive procedure for the diagnosis of pulmonary lesions including preinvasive and invasive malignancies. (Roby et al., 1990; Gupta and Garg 2006) Bronchoalveolar Lavage (BAL), which was initially developed as therapeutic tool has also gained acceptance and popularity as a tool for the diagnosis of lung cancer. (Gaur et al., 2007) Our aim was to study and compare the efficacy of Sputum cytology with BAL in the diagnosis of lung cancer by correlating them with histopathological diagnosis by bronchial biopsy.

MATERIALS AND METHODS

The study was carried out in the department of Pathology at ESICMC PGIMSR, Bangalore. Out of all clinically and radiologically suspected cases of lung cancer received from June 2010-June 2012(two years), i.e. 107, we selected 97 cases where sputum cytology, BAL and bronchoscopic biopsy were available. The case was not included when any one of the three samples are inadequate.

Histopathological diagnosis by bronchial biopsy was considered as gold standard. (Gaur et al., 2007) A fresh early morning sputum sample produced by deep cough was collected in a wide mouthed, shallow, sterile glass or plastic container for three consecutive days. The container was properly labelled and sealed with tight fitting lid. Four smears were made of each sample and stained with H&E, Papanicolaou, Leishmann and May Grunwald Giemsa (MGG) stains. Samples were regarded as satisfactory if alveolar macrophages were present. (Khalid et al., 2010) All slides were examined under microscope for malignant cells. BAL samples were obtained by flexible fiberoptic bronchoscopy done by the Pulmonologist. Samples were received in 20ml aliquots of normal saline in sterile vials. (Gaur et al., 2007) Samples were centrifuged and smears prepared with the sediment. Four smears were made and stained like that of sputum and were examined under microscope for malignant cells. The bronchoscopic biopsy was processed in an automated tissue processor and paraffin blocks were made. From each block three sections were taken at different levels and stained with H&E stain. Immunohistochemistry was done wherever required for confirmation. (Khalid et al., 2010) ‘z’ test of statistical significance was applied to compare the
effectiveness of Sputum Cytology with BAL in the diagnosis of lung cancer.

RESULTS

The study included 97 patients with clinically suspected lung cancer. Of these, 33 cases were subsequently confirmed as lung cancer by histopathologic evidence. Thus we have 33 confirmed cases of lung cancer in the present study. Out of 97 patients 79 were male and 18 were female with their age ranging from 50-79 years. The male: female ratio was 4.3:1. Age of the confirmed lung cancer patients were ranging from 50 to 72 years with mean of 60.8 years. A history of smoking more than fifteen cigarettes per day for longer than five years was given by 32 cancer patients. We thus have a striking majority of 96% smokers in cancer patients group. Sputum was positive for malignant cells in 10 cases (30%) and BAL cytology was positive in 23 cases (69.6%). There were no false positive cases. Distribution of different types of lung cancers and the percentage of positivity in each modality is described in Table 1 & 2. Radiological and bronchoscopic studies revealed a central or perihilar tumors in 11 cases of which 8 were positive for malignancy on sputum cytology giving a pick up rate of 72.7% for central lesions compared to 9% (2 cases) of 22 peripheral lesions. These pick up rate of 72.7% for central lesions compared to 9% (2 cases) of 22 peripheral lesions. Thus in these 33 cases the following radiological and bronchoscopic studies revealed a central or perihilar tumors in 11 cases of which 8 were positive for malignancy on sputum cytology giving a pick up rate of 72.7% for central lesions compared to 9% (2 cases) of 22 peripheral lesions. These pick up rate of 72.7% for central lesions compared to 9% (2 cases) of 22 peripheral lesions. Hence we conclude that a significant difference in proportions is there in between sputum cytology and BAL cytology. So BAL cytology is more effective diagnostic modality in comparison with sputum cytology in the diagnosis of lung cancer.

In the present study the age of the confirmed lung cancer patients were ranging from 50 to 72 years with mean of 60.8 years. 32 (96%) patients were smoker. In our study we noted that BAL cytology has high sensitivity of 69.6% in comparison to sputum cytology with 30% sensitivity, showing its superiority in the diagnosis of lung cancer. In a comparative study of BAL and open lung biopsy Yamamoto found that the results of these two to have a parallel relation except in few cases. (Yamamoto 1994)

There were no false positive cases in the present study. If cytology is suspicious or positive for malignancy, repeat cytology and clinical correlation with bronchoscopic and radiological findings is necessary. (Khalid et al., 2010) In the present study majority of the cases were of squamous cell carcinoma followed by adenocarcinoma and other types. Squamous cell carcinoma which is more frequently located in proximal bronchus showed positivity in thirteen cases in BAL cytology and eight cases by sputum cytology. Wongsurakiat et al. (1998) found that the diagnostic yield of BAL is influenced by the size and segmental location of the lesion. (Wongsurakiat et al., 1998) In our study radiologic and bronchoscopic studies revealed a central or perihilar tumors in 11 cases of which 8 were positive for malignancy on sputum cytology giving a pick up rate of 72.7% for central lesions compared to 9% (2 cases) of 22 peripheral lesions. These pick up rates are comparable to 85% as reported by Sing et al. (1997), 91% as reported by Khalid et al. (2010) and 71% as reported by Ammanagi et al. (2012) for perihilar tumors. A suspected case of small cell carcinoma of lung in BAL cytology was subsequently confirmed by Immunohistochemistry (chromogranin and synaptophysin) on bronchoscopic biopsy.

Table 1. Distribution of different types of lung cancer

<table>
<thead>
<tr>
<th>Type of Lung Cancer</th>
<th>Number of Cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous cell carcinoma</td>
<td>20</td>
<td>60.6</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>07</td>
<td>21.2</td>
</tr>
<tr>
<td>Small cell carcinoma</td>
<td>02</td>
<td>06.06</td>
</tr>
<tr>
<td>Large cell carcinoma</td>
<td>01</td>
<td>03</td>
</tr>
<tr>
<td>Neuroendocrine tumor</td>
<td>01</td>
<td>03</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>01</td>
<td>03</td>
</tr>
<tr>
<td>Plasmacytoma</td>
<td>01</td>
<td>03</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Comparison of effectiveness of BAL and Sputum cytology in different types of lung cancers

<table>
<thead>
<tr>
<th>Type of Lung Cancer</th>
<th>BAL* cytology</th>
<th>Sputum cytology</th>
<th>Biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous cell carcinoma</td>
<td>13</td>
<td>08</td>
<td>20</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>07</td>
<td>02</td>
<td>07</td>
</tr>
<tr>
<td>Small cell carcinoma</td>
<td>00</td>
<td>00</td>
<td>02</td>
</tr>
<tr>
<td>Large cell carcinoma</td>
<td>00</td>
<td>00</td>
<td>01</td>
</tr>
<tr>
<td>Neuroendocrine tumor</td>
<td>01</td>
<td>00</td>
<td>01</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>00</td>
<td>00</td>
<td>01</td>
</tr>
<tr>
<td>Plasmacytoma</td>
<td>01</td>
<td>00</td>
<td>01</td>
</tr>
<tr>
<td>Total</td>
<td>23(69.6%)</td>
<td>10(30%)</td>
<td>33</td>
</tr>
</tbody>
</table>

*Bronchoalveolar lavage

DISCUSSION

Lung cancer is an epidemic disease. Increasing evidence suggests that the screening and early detection may improve outcome in lung cancer. (Chaudhary et al., 2010) Sputum cytology is a definite diagnostic test for lung cancer. (Jay et al., 1980) Cytological examination of Papanicolaou stain of sputum is accepted as a useful diagnostic tool in lung cancer. (Ammanagi et al., 2012) In the present study sputum sample spontaneously produced by deep cough were brought without any fixatives. As delay in processing may lead to cellular degeneration, smears were prepared and examined as soon as possible. (Chaudhary et al., 2010; Thunnissen 2003; Tsang et al,1992; Neumann et al., 2009; Oswald et al., 1975) However Koss has suggested that the specimens with high mucin content like sputum can be preserved for 12-24 hours under refrigeration. (Myron et al., 2009) Advent of flexible fiber-optic bronchoscope has lead to new turn as samples like bronchial washing, BAL and transbronchial biopsy could be collected from the respiratory tract. (Ahmed and Ahmed 2004) BAL is a valuable diagnostic and research tool in pulmonology. (Kopinski et al., 2000) In a comparative study of BAL and open lung biopsy Yamamoto found that the results of these two to have a parallel relation except in few cases. (Yamamoto 1994)
With fairly good sensitivity BAL promises to be a convenient
cytological technique that can be confidently utilised for
screening of doubtful cases and early diagnosis of lung cancer
as it saves the time needed for the processing of the biopsy
specimens.

Conclusion

BAL cytology is significantly more effective in the diagnosis
of lung cancer in comparison to sputum cytology. As sputum
cytology is a simple, reliable, cost effective and non-invasive
procedure it can still be used as one of the diagnostic modality
for lung cancer with fairly good sensitivity.

REFERENCES

Ahmed A, Ahmed S. Comparison of bronchoalveolar lavage
cytology and transbronchial biopsy in the diagnosis of
carcinoma of lung. J Ayub Med College Abbottabad

Ammannagi AS, Dombale VD, Miskin AT, Dandagi GL,
Sangolli SS. Sputum cytology in suspected cases of
carcinoma of lung (Sputum cytology a poor man’s
bronchoscopy!). Lung India 2012; 29:19-23.

Chaudhary M, Younus M, Rehman A, Zafar S, Bukhari S. The
Importance of Sputum Cytology in the Diagnosis of Lung

Choi YD, Han CW, Kim JH, Oh JJ, Lee JS, Nam JH, et al.
Effectiveness of sputum cytology using ThinPrep method
for evalulation of lung cancer. Diagn Cytopathol 2008;

Gaur DS, Thapliyal NC, Kishore S, Pathak VP. Efficacy of
bronchoalveolar lavage and bronchial brush cytology in

Gupta KB, Garg S. Sputum induction - A useful tool in
diagnosis of respiratory diseases. Lung India 2006;
23:82-6.

Jay SJ, Wehr K, Nicholson DP, Smith AL. Diagnostic
sensitivity and specificity of pulmonary cytology-
comparison of techniques used in conjunction with flexible

Khalid M Ch, Younus M, Rehman AU, Zafar S, Bukhari SMH.
The Importance of Sputum Cytology in the Diagnosis of

Kopinski P, Chlap Z, Owsinski J, Soja J, Stankiewicz Z,
of material from bronchoalveolar lavage (BAL) for
cytoimmunologic examinations in interstitial lung

Myron R Melamed, Leonard G Koss. Diagnostic cytology- Its
origin and principles. In:Myron R Melamed, Leonard G
Koss, editor. Koss’ diagnostic cytology and its
histopathological basis, 5th ed. Philadelphia: Lippincott
Williams & Wilkins; 2009. p. 3-20.

Neumann T, Meyer M, Patten FW, Johnson FL, Erozan YS,
Frable WJ, et al. Premalignant and malignant cells in
sputum from lung cancer patients. Cancer 2009;117:473-
81.

Oswald NC, Hinson KF, Canti G, Husain OA, Girling DJ, Tall
R, et al. Survey of the sputum cytology service in England

Roby TJ, Swan GE, Sorensen KW, Hubbard GA, Schumann
GB. Discriminant analysis of lower respiratory tract
components associated with cigarette smoking based on
quantitative sputum cytology. Acta Cytol 1990; 34:147-
54.

Sing A, Freudenberg N, Kortsik C, Wertzal H, Klosa B, Hasse
J. Comparison of the sensitivity of sputum and brush
cytology in the diagnosis of lung carcinomas. Acta Cytol
1997;41:399-408.

Thunnnissen FB. Sputum examination for early detection of

Tsang KW, Bentley AM, Mann JS, Belcher J, Pantin CF.
Survey of outpatient sputum cytology- Influence of written
instructions on sample quality and who benefits from

Wongsurakiat P, Wongbunnate S, Dejsomtrut ai W,
Diagnostic value of bronchoalveolar lavage and
postbronchoscopic sputum cytology in peripheral lung

Yamamoto S. Diagnostic value of bronchoalveolar lavage
(BAL)-the comparative study with open lung biopsy and