Comparison of bronchial biopsy, broncho alveolar lavage (BAL), brush cytology and imprint cytology in suspected cases of lung cancer

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Abstract
Background: The use of cytological methods in the diagnosis of malignant lesions of the respiratory tract has been generally acclaimed as one of its most successful applications. Flexible fiberoptic bronchoscopy revolutionized respiratory cytology, as bronchial brushings, broncho-alveolar lavage and bronchial forceps biopsy became more easy, accessible and popular, shifting the emphasis from diagnosis of advanced malignancy in inoperable patients to the use of cytology as a first line diagnostic and management tool. Respiratory tract cytology is well established throughout the world as a diagnostic procedure in the evaluation of patient with suspected lung malignancy.

Methodology: The present study compromises of bronchoscopic cytology and histology of bronchial biopsy in 80 patients suspected of lung tumors. The study was carried out in the department of pathology M.P. shah medical college and the samples of the bronchoscopic material were received from tuberculosis and chest department of G.G hospital Jamnagar.

Results: Out of 80 patients 66 were found to be malignant. Some of the suspicious lesions turned out to be malignant in biopsy. In the carcinoma of lung squamous cell carcinoma was the most common carcinoma (39.39%) followed by adenocarcinoma (21.21%) small cell carcinoma 13.63% and large cell carcinoma 7.57%, majority of the cases 77.5 % were male predominat.

Conclusion: Pulmonary cytology is an important, basic diagnostic tool for the detection of lung cancer, that too in early diagnosis. Fibroptic bronchoscopy is an easy, OPD procedure which is minimally invasive and without any risk. It provides direct visualization of respiratory tract as well as lesion proper and variety of specimens can be collected.

Keywords: Bronchial biopsy, Broncho alveolar lavage (BAL), Brush cytology and Imprint cytology, Lung cancer

1. Introduction

Pulmonary cancers have taken place as most common malignant disease affecting larger population with continuous rising incidences and currently recognized as serious health problem because of its high morbidity and mortality and poor prognosis¹.

The use of cytological method In the diagnosis of malignant lesions of respiratory track has been generally acclaimed as one of its most successful applications².

Tumors of lung as noted by alder, were a rarity in the beginning of the twentieth century. There was no way for alder to foresee that in the coming years cancer of lung would show a astonishing 15 fold increase in males and 10 fold
increase in females. In females, cancer of lung is expected to surpass the deaths due to cancer of breast\(^3\).

The global incidence of lung cancer is increasing at the rate of 0.5 % per year and is the leading cause of death in most countries. Smoking is considered to be the cause of 85 % of deaths due to lung cancer death\(^4,5\).

The result of the American society’s prevention study II indicates that the risk of lung cancer has doubled among men and more than quadrupled in females, in comparison with prior estimates. Rosenow stated that even if all the smokers stopped smoking immediately, no decline in lung cancer incidences for 5 – 15 years\(^6\).

The age and sex distribution for various histological subtypes of lung has been shifted during the past several decades\(^7\).

So, early detection is deadly needed in present scenario with clinical symptoms, x-ray chest, sputum cytology and tumor markers which can support the evidence of tumor by histological cell typing. Therefore endoscopies and biopsies become inevitable since the advent of flexible fiberoptic bronchoscope by Ikeda in the early 1970\(^8\).

Accuracy in the diagnosis of lung tumors has increased with the introduction of radiological guided per cutaneous transthoracic needle biopsy. Though the histological diagnosis of lung cancer from these specimens is considered definitive it is useful to have an earlier indication as to the presence of malignancy and the cytomorphological analysis of touch imprint smears made from core biopsies of the lesions might advance this\(^9\).

Thoractomy followed by removal of mass confirmed further for definitive diagnosis where thoracic surgeon and unit is available, raises the confidence level of the pathologist with compliance of the procedure.

2. Material and Method

The present study compromises of bronchoscopic cytology and histology of bronchial biopsy in 80 patients suspected of lung tumors. The study was carried out in the department of pathology M.P. Shah Medical college and the samples of the bronchoscopic material were received from tuberculosis and chest department of G.G hospital Jamnagar.

Total 80 patients clinically suspected of lung cancer were selected for cytological and histological study during the period of Nov 2004 to Nov 2006.

The bronchoscopy was performed by flexible fiberoptic bronchoscope in tuberculosis and chest department in G.G hospital Jamnagar.

3. Imprint Cytology

3.1 Procedure

The specimen of bronchial biopsy, before putting in a formalin bottle, was put on a clear glass slide, with the help of the other clear slide the imprint of biopsy was taken.

The side of the biopsy than changed and another imprint was taken on the same previous slide but on the other side.

The smears were fixed with 95% ethyl alcohol for 15 minutes. The well fixed slides were stained with haematoxylin and eosin.

The same biopsy bit was subjected for routine paraffin sections and stained by haematoxylin and eosin stain and histopathological correlation was done on subsequent days.

Fixed smears of TBNA and brush smears, collected by chest physician at T.B and chest department, were received and stained.

3.2 Staining

Haematoxylin and eosin and papanicolaou stain have been used.

4. Observations and Result

The present study comprises of 80 patients of suspected lung cancer during the period of Nov 2004 to Nov 2006. The patients included in this study had suspicious radiological as well as clinical findings of lung cancer with sputum
examination, suspicious for malignant cells. The study is of bronchoscopic specimens i.e is bronchial biopsy and its imprint cytology, bronchial brushing and TBNA.

4.1 Diagnosis yield for positivity of malignancy by various methods

In the present study, bronchoscopy was performed in 80 cases and bronchial biopsy specimens were studied in 80 cases. Touch preparation were examined in all the 80 cases. TBNA collection were received in 50 cases and brush smears were received in 42 cases. The cases where bronchial biopsy was not taken were excluded from the study.

Material yield by various cytological technique obtained through bronchoscope and diagnostic positivity for malignancy observed as follows:

**Table 01 Material yield and diagnostic positivity for malignancy by various bronchiscopic techniques:**

| Techniques | No of specimens | Inadequate material no of cases | Material yield no of cases | Positive for malignancy no of cases |
|------------|----------------|--------------------------------|---------------------------|---------------------------------|
| Brush      | 42             | 07                             | 35 (83.3 %)               | 27                              |
| TBNA       | 50             | 13                             | 37 (74.0%)                | 26                              |
| IMPRINT    | 80             | 04                             | 76 (95%)                  | 58                              |
| Biopsy     | 80             | 06                             | 74 (92.5%)                | 66                              |

Thus mentioned in the above table maximum material yield (95%) was in the imprint smear, followed by brush cytology (83.3 %). Biopsy material found to be inadequate as mentioned in the table (92.5 %) this cases confirmed by other modalities, particularly imprint smears.

**Table 02 : Showing cytological findings by various techniques**

| NO | CATEGORY               | BRUSH n=42 | TBNA n=50 | IMPRINT n = 80 | BIOPSY n=80 |
|----|------------------------|------------|-----------|----------------|-------------|
| 1  | Definitive malignancy  | 27         | 26        | 58             | 66          |
| 2  | Suspicious for malignancy | 04       | 05        | 06             | 02          |
| 3  | Dysplasia              | 02         | 02        | 04             | 02          |
| 4  | Non malignant          | 02         | 04        | 08             | 04          |
| 5  | Inadequate             | 07         | 13        | 04             | 06          |

Out of 80 patients 66 were found to be malignant. Some of the suspicious lesions turned out to be malignant in biopsy. Some of the smears which were found to be reactive due to irritation and chronic infection. All the lesions were classified accordingly to their cytomorphology and histology as mentioned in the table III.

**Table 03 Incidence of various types of lung tumors**

| No | Type of tumor               | No of cases | Percentage % |
|----|-----------------------------|-------------|--------------|
| 1  | squamous cell carcinoma     | 26          | 39.39        |
| 2  | Adenocarcinoma              | 14          | 21.21        |
| 3  | Small cell carcinoma        | 09          | 13.63        |
| 4  | Large cell carcinoma        | 05          | 7.57         |
| 5  | Bronchiole alveolar carcinoma | 03       | 4.54         |
| 6  | Adenosquamous carcinoma      | 02          | 3.03         |
| 7  | Metastatic carcinoma        | 04          | 6.06         |
| 8  | Undifferentiated carcinoma  | 03          | 4.54         |
|    | Total                       | 66          | 100          |

From table No.3, it was observed that squamous cell carcinoma was the most common carcinoma (39.39%) followed by adenocarcinoma (21.21%) small cell carcinoma 13.63% and large cell carcinoma 7.57%.
Table :04 Age incidence in different carcinomas

| NO | LUNG CANCER                  | 31-40 | 41-50 | 51-60 | 61-70 |
|----|----------------------------|-------|-------|-------|-------|
| 1  | Squamous cell carcinoma    | 01    | 01    | 10    | 14    |
| 2  | Small cell carcinoma       | 01    | 01    | 02    | 05    |
| 3  | Adenocarcinoma             | -     | 03    | 06    | 05    |
| 4  | Bronchiolo alveolar carcinoma | -   | -     | 03    | -     |
| 5  | Large cell carcinoma       | 01    | -     | 01    | 03    |
| 6  | Adenosquamous carcinoma    | -     | -     | 01    | 01    |
| 7  | Metastatic carcinoma       | -     | -     | 04    | -     |
| 8  | Undifferentiated carcinoma | 01    | -     | -     | 02    |
|    | Total                      | 04    | 05    | 27    | 30    |

From table no 04, observed that, majority of the cases were in the 6th and 7th decade of life. Malignancy was common in the 6th and 7th decade for primary lesion while metastatic lesion were common in 6th decade of life.

Table :05 Overall gender incidence in 80 cases of study

| No | Sex of the Patients | No of Cases | Percentage |
|----|---------------------|-------------|------------|
| 1  | Male                | 62          | 77.5       |
| 2  | Female              | 18          | 22.5       |
|    | Total               | 80          | 100%       |

From table no 05, observed that, majority of the cases 77.5 % were male predominant.

Table :06 Positive history of smoking (N= 80)

| No | History of smoking       | No of cases | M  | F  | Percentage |
|----|--------------------------|-------------|----|----|------------|
| 1  | Positive history of smoking | 67          | 62 | 05 | 83.75      |
| 2  | Negative history of smoking | 13          | 05 | 08 | 16.25      |
|    | Total                    | 80          | 13 | 100|            |

From Table no 06 Shows out of 80 patients studied, 67 had positive history of smoking. 62 were Male and 05 were female.

Table :07 Positivity history of smoking in lung cancer patient (N =66)

| No | History of smoking       | No of Patient | Percentage |
|----|--------------------------|---------------|------------|
| 1  | Positive history of smoking | 58 (55M +3F) | 87.88      |
| 2  | Negative history of smoking | 08           | 12.12      |
|    | Total                    | 66           | 100        |

From table no 07 shows out of 66 lung cancer patients, 58 (87.88%) patients had positive history of smoking. 3 of them were female.

Table :08 Statistical analysis of various bronchiscopy techniques

| Technique | TP | FP | TN | FN | Sensitivity | Specificity | PVPR | PVNR | Accuracy Rate |
|-----------|----|----|----|----|-------------|-------------|------|------|---------------|
| BRUSH     | 23 | 03 | 06 | 03 | 88.46       | 66.67       | 88.46| 66.67| 82.85         |
| TBNA      | 22 | 05 | 08 | 02 | 91.60       | 61.53       | 81.48| 80.8 | 81.08         |
| IMPRINT   | 62 | 02 | 15 | 01 | 98.41       | 88.23       | 96.87| 93.75| 92.50         |
| BIOPSY    | 51 | 00 | 13 | 02 | 96.83       | 100         | 100  | 86.70| 97.37         |
From table no 08, it was observed that imprint cytology had highest sensitivity (98.41%) and highest PVNR (93.75%), while bronchial biopsy had 96.83% sensitivity and 86.70% PVNR.

Table : 09 Statistical analysis of various bronchiscopy techniques

| Technique | TP  | FP  | TN  | FN  | Sensitivity | Specificity | PVPR | PVNR | Accuracy Rate |
|-----------|-----|-----|-----|-----|-------------|-------------|------|------|---------------|
| BRUSH     | 23  | 03  | 06  | 03  | 88.46       | 66.67       | 88.46| 66.67| 82.85         |
| TBNA      | 22  | 05  | 08  | 02  | 91.60       | 61.53       | 81.48| 80.8 | 81.08         |
| IMPRINT   | 62  | 02  | 15  | 01  | 98.41       | 88.23       | 96.87| 93.75| 92.50         |
| BIOPSY    | 51  | 00  | 13  | 02  | 96.83       | 100         | 100  | 86.70| 97.37         |

TP : TRUE POSITIVE; TN : TRUE NEGATIVE; FP : FALSE POSITIVE; FN : FALSE NEGATIVE; PVPR: PREDICTIVE VALUES OF POSITIVE RESULTS; PVNR : PREDICTIVE VALUES OF NEGATIVE RESULT

5. Discussion

Because primary and secondary tumors if ling are such a frequent phenomenon, we must find reliable diagnostic methods with a high yield of positive results and accurate identification of the tumor type.

Table :10 Percentage incidence of various types of lung cancers

| Author              | Squamous cell carcinoma | Adeno. carcinoma | Bronchiolo Alveolar carcinoma | Small cell carcinoma | Large cell carcinoma | Undiff. carcinoma | Others |
|---------------------|-------------------------|------------------|-------------------------------|----------------------|----------------------|-------------------|--------|
| Agarwal et al10     | 55                      | 21.5             | 1.08                          | 10.88                | -                    | 5.89              | 5.65   |
| Rosell et al11      | 37.8                    | 14.2             | 2.86                          | 11.0                 | 8.50                 | -                 | 7.34   |
| Popp et al12        | 31.57                   | 8.23             | 3.53                          | 8.05                 | -                    | 3.20              | -      |
| Paulose et al13     | 40.0                    | 15.8             | 3.94                          | 15.54                | 5.7                  | -                 | 8.20   |
| Joos et al14        | 34.45                   | 18.2             | 5.0                           | 11.10                | 10.1                 | -                 | -      |
| Adnan et al15       | 31.57                   | 25.3             | -                             | -                    | 12.4                 | 7.2               | 5.4    |
| Present study       | 39.39                   | 21.21            | 4.54                          | 13.63                | 7.57                 | 4.54              | 6.06   |

From the above table, it was observed that the squamous cell carcinoma was the most common type of lung cancer (39.39%) followed by Adenocarcinoma (21.21%) and Small cell carcinoma (13.63%) which is quite comparative with other studies.

Table : 11 Showing statistical comparison of bronchial biopsy

| Author              | Sensitivity | specificity | PPV   | NPV   | Accuracy rate |
|---------------------|-------------|-------------|-------|-------|---------------|
| Matsuda et al16     | -           | 98.0        | -     | -     | -             |
| Adnan et al15       | 90.5        | -           | -     | -     | 84.0          |
| Rosell et al11      | -           | 95.0        | -     | -     | -             |
| Govert et al17      | 95.0        | -           | 97    | -     | 95.7          |
| Paulose et al13     | 85.0        | 100         | -     | -     | -             |
| Present study       | 96.83       | 100         | 100   | 86.70 | 93.37         |

The above table shows that, the sensitivity, specificity and accuracy rate of bronchial biopsy was 96.83, 100 and 93.37% respectively, which is quite comparable with other studies.

6. Conclusion

- Pulmonary cytology is an important, basic diagnostic tool for the detection of lung cancer, that too in early diagnosis.
- Fibroptic bronchoscopy is an easy, OPD procedure which is minimally invasive and without any risk. It provides
direct visualization of respiratory tract as well as lesion proper and variety of specimens can be collected.

- Imprint cytology is a rapid, reliable and inexpensive method, which does not require any extra procedure and provides an additional support to histologic examination.
- Technique of imprint cytology is simple, cost effective and rapid which appears more reliable than frozen section preparation, which requires more expertise trained persons for preparation and cost of maintenance of instrument as well.
- Combined use of bronchial brush, TBNA, imprint cytology and bronchial biopsy increases the accuracy and sensitivity of the diagnosis than use the single technique only.
- Imprint smears of trans-thoracic core biopsy helps to enhance diagnostic accuracy, whenever available.

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