Utility of Image Guided Fine Needle Aspiration Cytology in Intra-Thoracic Lesions with Emphasis on Lung Cancer Detection

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Abstract

Background and Aims: Fine Needle aspiration cytology has emerged as an essential pre-biopsy investigation to rule out or confirm malignancy in superficial as well as deep seated lesions. Radiological assistance has proved to be a blessing for obtaining adequate samples. With unwavering leading position of lung cancer in terms of incidence and mortality, it has become necessary to study the trends of our population and assess the usefulness of techniques aiding in early diagnosis. The objective is to obtain prevalence of lung cancer and utility of various methods in obtaining cytological material for assessment in intrathoracic lesions. Material and Methods: We conducted an observational analytic study at a tertiary care teaching hospital over a period of 3.5 years including a total of 307 patients with suspected lung malignancy. Samples were collected using image guided techniques including Fibre-optic bronchoscopy (FOB), Ultra-sonography (USG) and Computed tomography (CT). The smears were processed as per standard institutional protocol and were evaluated by a senior pathologist. Results: Squamous cell carcinoma was the most frequent type of Primary lung malignancy, followed by adenocarcinoma. The malignancies were more common in males and in age group of 61 to 70 years. Conclusion: Respiratory cytology remains the initial mode of investigation in intra-thoracic malignancies. The high sensitivity, low-cost and rapidity of the results works its advantages for both the patient and the clinician. High cellular yield obtained with the use of trans-bronchial needle aspiration and bronchial brushing rationalizes their use as a screening test to establish both malignant as well as non-malignant diagnoses. Further improvement in utilization of the available modalities and addition of ancillary testing can reduce the need of invasive procedures.

Keywords: Fine needle aspiration cytology, image-guided, intra-thoracic, lung cancer

INTRODUCTION

Fine needle aspiration cytology (FNA) is an extensively used tool for cytological evaluation of superficially palpable as well as radiologically confirmed deep-seated intra-thoracic lesions.[1] Advanced imaging techniques like Fibre-optic bronchoscopy, Computed Tomography (CT), Ultra-sound and Magnetic Resonance Imaging (MRI) make it possible to obtain samples adequately from difficult to reach intra-thoracic as well as intra-abdominal organs. Precise localisation of needle in the lesion under real-time visualization, rapid, painless and cost-effective, high accuracy and low complication rates makes this procedure one of the initial choices in evaluating the suspicious mass lesions.

GLOBOCAN 2018 data reveals that current worldwide burden of lung cancer is 11.6% (2.094 million) and mortality is 18.4% (1.8 million) of all new cases of malignancies in both sexes and all ages, which is the highest of all.[2] We conducted this study to assess the burden and population trends of this disease among the patients presenting at our tertiary care centre and utility of diagnostic methods available at our center.

METHODS

We conducted an observational analytic study at a tertiary care centre, over a period of 3.5 years from January 2015 to June 2018. Patients presenting with radiologically detected mass lesions, including those arising from chest-wall, lungs, mediastinal lymph nodes and thymus were included in the
study. Patients with suspicion of malignancy but no visible mass on bronchoscopy or radiologically, and patients with lesions close to large blood vessels were excluded from the study. Approval was obtained from institutional ethical committee prior to conducting the study [Ethical clearance Letter no. 268/Acad-III/MCA/2018].

Detailed clinical data was obtained and radiological findings were noted. Informed patient consent was obtained from the patient prior to the procedure. Samples were collected using image guided techniques including Fibre-optic bronchoscopy (FOB), Ultra-sonography (USG) and Computed tomography (CT).

Needle aspiration samples were obtained by FOB for bronchoscopically visible lesions along with bronchoalveolar lavage fluid and sputum, for correlation. Bronchial biopsy was also done in few cases with strong suspicion of malignancy. Ultrasound guided cytology samples were obtained for peri-pheraly located lung parenchymal lesions and pleural lesions. CT guided samples were obtained for mediastinal lesions including thymus, mediastinal lymph nodes and deep seated parenchymal lesions. A minimum of 2-3 smears were prepared. Bronchoalveolar lavage fluid and sputum samples were obtained simultaneously. Smears were processed using standard protocol. Air-dried smears were stained with May Grunwald’s Giemsa (MGG) stain and alcohol-fixed smears were stained with Hematoxylin and Eosin (H&E) stain. Special stains like Papanicolaou (PAP) and Periodic Acid Schiff (PAS) stain were used as and when required to establish definitive diagnosis. All the smears were assessed by a single senior pathologist, removing the possibility of inter-observer bias. The data obtained was analysed by SPSS 20.0 software. Microsoft word and excel was used to assimilate the data and prepare the article.

**Results**

We performed a total of 307 Fine needle aspirations. 278 samples (90.55%) were obtained from the parenchyma of both lungs, 11 samples (3.58%) each were obtained from mediastinum and pleura, 3 samples (0.98%) each were obtained from bilateral lungs and bronchi, and 1 sample (0.33%) was obtained from chest wall. The most common site was right lung (135 cases, 43.97%), followed by left lung (125 cases, 40.72%). 252 cases (82.08%) were seen in males and 55 cases (17.92%) were seen in females. Male to female patient ratio was 4.58:1. Youngest patient included in our study was 17 years old and the oldest was 86 years old, with mean age at presentation being 58.14 ± 13.13 years.

Most common mode of technique was Fibre-optic bronchoscopy (229 cases, 74.60%), computed tomography (60 cases, 19.54%) and Ultrasound (18 cases, 5.86%).

Out of 307 cases most commonly diagnosed lesions in both the genders were malignancies in 148 cases (48.21%) including 124 males (83.78%) and 24 female (16.21%) patients, followed by inflammatory lesions in 74 cases (24.10%) including 60 male (81.08%) patients and 14 female (18.92%) patients. A total of 15 cases (4.89%) were inconclusive, and majority were due to inadequate sample material obtained on FNAC [Table 1].

Out of 148 cases, most malignancies were reported between the age group of 61 to 70 years of age (58 cases; 39.19%), followed by 51 to 60 years age (40 cases; 27.03%). Out of 74 cases of inflammatory lesions majority were seen between 51 to 60 years of age (26 cases; 35.14%), followed by 61 to 70 years (20 cases; 27.03%). The age range was 22 years to 85 years.

All types of lung carcinoma were found more commonly in males than in females. Out of total 128 primary lung lesions, the most common primary lung malignancy reported was Squamous cell carcinoma in 55 cases (42.97%) [Figure 1]. 46 cases (38.64%) in males and 9 cases (16.36%) in females.

| S. No. | Diagnosis | Male | Male % | Female | Female % | Total (%) |
|-------|-----------|------|--------|--------|----------|-----------|
| 1     | Normal    | 26   | 78.79% | 7      | 21.21%   | 33 (10.75%) |
| 2     | Inflammatory | 60   | 81.08% | 14     | 18.92%   | 74 (24.10%) |
| 3     | Benign    | 15   | 83.33% | 3      | 16.66%   | 18 (5.86%) |
| 4     | Malignant | 124  | 83.78% | 24     | 16.21%   | 148 (48.21%) |
| 5     | Suspicious for malignancy | 15   | 78.95% | 4      | 21.05%   | 19 (6.19%) |
| 6     | Inconclusive | 12   | 80.00% | 3      | 20.00%   | 15 (4.89%) |
| TOTAL |           | 252  | 55     | 307    | 100%     |

**Figure 1:** Squamous cell carcinoma of lung- Malignant squamous cells are seen in clusters as well as singly, with well-defined borders, dense eosinophilic cytoplasm, high N: C ratio with hyperchromatic nuclei against necrotic background. (H&E; 200x)
The second most frequently reported malignancy was Adenocarcinoma of lung (41 cases; 32.03%) [Figure 2], 37 cases (90.24%) were seen in male patients, while 4 cases (9.76%) were seen in female patients. The least common cases were of Adeno-squamous carcinoma, large cell carcinoma and malignant mesothelioma with one case (0.78%) each [Table 2].

All the 3 major types of lung carcinoma—Squamous cell carcinoma, Adenocarcinoma and Small cell carcinoma—were most frequently seen in the seventh decade of life (50 cases; 39.06%), followed by patients presenting in 6th decade (34 cases; 26.56%) [Table 3].

Lung is one of the commonest recipients of haematologically disseminating malignancies from all sites of body. We recorded a total of 12 cases of secondary malignancies. Lung was equally common site for secondaries in both squamous as well as Adenocarcinoma (3 cases; 25% each). 2 cases (16.67%) were of metastatic Papillary carcinoma of Thyroid. One case each (8.33%) of Metastatic spindle cell sarcoma, Metastatic chondrosarcoma, Metastatic deposits of ductal carcinoma of breast and metastatic deposits of Seminoma were noted.

The most common complaint of patients was dyspnoea (222 cases, 72.31%), followed by cough (194 cases, 63.19%). The least common complaint was weight loss (only 50 cases, 16.29%). Average duration of symptoms was 7.9 ± 9.88 weeks. Histopathology was performed on 88 cases, among them 80 cases (90.91%) correlated positively with the cytological diagnosis.

**Discussion**

Lung cancer has seen rising incidence for many years. In our opinion, it is imperative to study the population trends of lung cancer to understand its demographic distribution, possible modalities for screening, early diagnosis and appropriate management. It is one of the cancers that has targeted therapy available, thus cytological diagnosis can help in the early and appropriate clinical decision making of further management plan.

In our study overall Male: Female ratio of intra-thoracic FNACs was 4.58:1. This was closely similar to the study conducted by Singh et al. (4.43:1), Jindal et al. (5.2:1), and Prasad et al. (5.58:1). 

International studies done by Roth et al., Kabir et al. and Sagerup et al. reported a lower M:F ratio of 1.56:1, 1.85:1 and 1.5:1, respectively, with slight male predominance. This indicates relatively higher prevalence of pulmonary malignancies in female subjects in western world. Overall, all studies showed predominance of male patients, which is likely due to higher incidence of smoking in males.

Majority of the cases in our study were found in the age group of 61 to 70 years, which was similar to outcomes of Gaur et al. who reported majority of the lung malignancies in the same age group. Singh et al., Jindal et al., Kumari et al., and Kumari et al. reported most malignancies between 51 to 60 years age group.

Mean age of patients in our study (58.14 years) was found to be similar to studies conducted by Singh et al. (57.9 years) and Tuladhar et al. (59.0 years).

Squamous cell carcinoma of lung was the most common intra-thoracic malignancy in our study (42.97%). Studies conducted by Singh et al., Kumari et al., Tuladhar et al., Kaushal et al., Rangaswamy et al., Shobha et al. and Bodh et al. also reported Squamous cell carcinoma to be the most common primary intra-thoracic malignancy.

Tuladhar et al. reported higher incidence of Squamous cell carcinoma (51%) compared to our study. The least common
Table 3: Age-wise distribution of Primary Lung malignancies

| Diagnosis                  | 11-20 yrs | 21-30 yrs | 31-40 yrs | 41-50 yrs | 51-60 yrs | 61-70 yrs | >70 yrs | Total |
|----------------------------|-----------|-----------|-----------|-----------|-----------|-----------|---------|-------|
| Squamous cell carcinoma    | 6 (11.32%)| 2 (1.82%) | 11 (22.45)| 28 (56.90)| 10 (20.41)| 14 (28.80)| 11 (22.45)| 75    |
| Adenocarcinoma             | 3 (5.88%) | 4 (3.64%) | 14 (28.80)| 16 (32.00)| 4 (8.16%) | 9 (18.37)| 2 (4.08%)| 49    |
| Small cell carcinoma       | 0 (0%)    | 1 (0.94%) | 4 (8.16%) | 8 (16.00%)| 2 (4.08%) | 3 (6.12%)| 0 (0%)  | 17    |
| Adenosquamous carcinoma    | 0 (0%)    | 0 (0%)    | 1 (0.94%) | 1 (0.94%) | 0 (0%)    | 0 (0%)  | 1 (0.94%)| 2     |
| Large cell carcinoma       | 5 (9.43%) | 8 (7.27%) | 15 (30.51)| 5 (10.00%)| 0 (0%)    | 0 (0%)  | 0 (0%)  | 35    |
| Poorly differentiated carcinoma | 7 (13.51)| 9 (8.24%) | 7 (14.29%)| 6 (12.00%)| 0 (0%)    | 0 (0%)  | 0 (0%)  | 23    |
| Undifferentiated carcinoma | 0 (0%)    | 2 (1.82%) | 1 (0.94%) | 2 (3.92%) | 1 (2.04%) | 3 (6.12%)| 0 (0%)  | 10    |
| Malignant mesothelioma     | 1 (1.92%) | 1 (0.94%) | 3 (6.12%) | 4 (7.87%) | 1 (2.04%) | 0 (0%)  | 0 (0%)  | 9     |

Total (%) 0 (0%) 1 (0.78%) 3 (2.34%) 18 (14.06%) 34 (26.56%) 50 (39.06%) 22 (17.18%) 128 (100%)

Table 4: Sensitivity, Specificity, PPV, NPV and Accuracy of Trans-Bronchial Needle aspiration (TBNA), Bronchoalveolar lavage (BAL) and sputum

| Type of Specimen                  | Sensitivity | Specificity | PPV    | NPV    | Accuracy |
|-----------------------------------|-------------|-------------|--------|--------|----------|
| Trans-bronchial Needle aspiration/ Bronchial Brushing | 100%        | 21.5%       | 89.6%  | 100%   | 89.71%   |
| Broncho-alveolar Lavage fluid     | 48.15%      | 100%        | 100%   | 17.65% | 53.33%   |
| Sputum                            | 32.26%      | 85.71%      | 90.91% | 22.22% | 42.11%   |

incidence of Squamous cell carcinoma (6.67%) was reported by Kulkarni et al., who reported Adenocarcinoma lung to be the most common primary malignancy (70%).

Adenocarcinoma lung was the second most common malignancy in our study (32.03%) and Small cell carcinoma was the third most common malignancy (13.28%). Our results were similar to studies conducted by Singh et al., Kumari et al. and Rangaswamy et al., who reported Adenocarcinoma lung to be second most common primary lung malignancy at 26.0%, 19.35% and 25%, respectively and Small cell carcinoma to be the third most common malignancy at 18.4%, 3.22% and 15.38%, respectively.

Gaur et al., Tuladhar et al., Kaushal et al. and Bodh et al. reported Small cell carcinoma to be more common than Adenocarcinoma, which was discordant with our findings.

Sensitivity and Specificity of TBNA cytology in our study was 100% and 21.5%, respectively [Table 4]. Accuracy of diagnosis from a TBNA sample in our study was 89.71%. Histopathology was used as the gold standard test for calculating sensitivity, specificity, PPV, NPV and accuracy of various cytological samples. These Findings were closely similar to studies conducted by Singh et al. and Kulkarni et al.

Singh et al. conducted a CT guided trans-bronchial needle aspiration cytology study in 2004 and reported higher sensitivity, specificity and accuracy compared to all other studies. This indicated better diagnostic outcomes with use of CT guidance for improved precision sampling. Similar outcome was reported in our study.

The yield of TBNA cytology in our study was similar to yield of cytology performed by Kulkarni et al. (2014) in their study. While many studies reported a lower yield compared to our study. Expertise of performing the technique can affect the yield outcomes. TBNA and bronchial brushing focus on obtaining sample from a small area of suspicion, thus the sample gives better cellular yield from the suspected pathology. While samples from bronchoalveolar lavage and sputum samples provide cellularity from a wider area and includes more normal cellularity compared to TBNA samples and bronchial brushings. Cases where histological outcomes were different from the initial cytopathology outcomes was likely due to inherent limitations of cytopathology like non-representative sample, poor sample preservation, processing artefacts, obscuring factors like blood, inflammatory cells and mucous. The cell morphology can be variable in lesions of similar categories.

The purpose of our study and studies done by previous authors remains to be focused on a common aim of improving patient management outcomes and reducing mortality. Image Guided Fine Needle Aspiration is a very useful, cost-effective method of initial investigation in patients presenting with symptoms of mass lesion in intra-thoracic or intra-abdominal region. Image guidance helps in targeting the needle at the appropriate site, therefore small lesions can be evaluated and false negative results can be avoided. Yet, this useful investigation remains under-used due to inherent difficulties of the procedure, time constraints in high patient volume setups and requirement of co-ordination between pulmonologist, pathologist and radiologist.

Differentiation between non-malignant and malignant mass lesions on the basis of cytological picture, can help in institution of accurate management and therapeutic protocols affecting the patient prognosis, while the results of advanced investigations like immunohistochemistry and flow cytometry are awaited. Malignancies can be confirmed or excluded in potentially operable lesions and thus the extent of surgery can be planned well in advance. There is an
additional advantage of submitting the cytology sample for ancillary tests like immunological, cytochemical, cytogenetic and microbiological investigations as and when necessary. Histology, though time consuming, remains as the gold standard investigation.

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Conflicts of interest
There are no conflicts of interest.

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