Original Article

A Study of Fine Needle Aspiration Cytology and Biopsy of Thoracic Masses with Special Reference to Clinical Staging and Performance Status of Patients with Lung Cancer

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Abstract

Background. Intra-thoracic mass is a common presentation in the chest out-patient department necessitating diagnostic procedures, like fine needle aspiration cytology (FNAC) and biopsy with variable results and complications. The present study was designed to study the clinical, cytopathological, histopathological spectrum of thoracic mass lesions and evaluation of complications arising out of these procedures.

Methods. One hundred-and-twenty patients were studied in respect to clinical and radiological data, computed tomography (CT) guided FNAC (n=120); subsequently 88 of these patients underwent core needle biopsy and 12 bronchoscopic biopsies were done. In all the patients with bronchogenic carcinoma, clinical staging and Eastern Cooperative Oncology Group (ECOG) scoring were done.

Results. Computed tomography guided FNAC (n=120) yielded positive results in 110 cases and subsequently biopsy was done in 100 cases; 92.5% cases were malignant, 5% were benign, and 2.5% were of infective aetiology. Overall sensitivity of CT-guided FNAC was found to be 91.7%; however, the sensitivity for anterior mediastinal mass was 75%. Adenocarcinoma was the most common malignancy (36.6%). Cytology and histopathology showed good concordance. Most of the patients with malignancy presented with late stage (ECOG 3 or more). Pneumothorax developed in 2.5% cases following FNAC and in 6.6% cases following biopsy.

Conclusions. Adenocarcinoma was found to be the most common primary lung cancer. FNAC had a high sensitivity with high concordance with histopathology. Pneumothorax is an infrequent complication of FNAC and true-cut biopsies.
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Key words: Thoracic mass, Computed tomography, FNAC, Biopsy, Adenocarcinoma, Pneumothorax.

Introduction

Thoracic mass (>30mm) is a common finding in patients attending respiratory medicine out-patient department. Though lung cancer is the most common cause for a thoracic mass, benign aetiologies, such as teratoma, lipoma, spindle cell tumour or infective aetiologies, such as tuberculosis, aspergilloma also present as thoracic masses. Benign neoplasms of the lung comprise less than one percent of all resected lung tumours.[1]

The Eastern Cooperative Oncology Group (ECOG) scale of performance status is widely used to quantify the functional status of cancer patients, and is an important factor determining prognosis in a number of malignant conditions. Performance status is the most powerful independent prognostic factor in advanced non-small cell lung cancer (NSCLC).[2]

Biopsy has always been a "gold standard" for the diagnosis of thoracic mass lesions. It enables one to get enough tissue for histopathological examinations as well as for other ancillary tests. On the other hand, fine-needle aspiration cytology (FNAC) is a simple, relatively safe, rapid, reliable technique for the diagnosis of pulmonary mass lesions, particularly with the aid of computed tomography (CT).

A prospective study was done to evaluate the clinical spectrum of thoracic mass lesion with FNAC and biopsy. We also evaluated the clinical stage and ECOG score of the subset of the patient with primary lung cancer and looked into the complications arising out of the invasive procedures done for the diagnosis.

Material and Methods

An observational, cross-sectional study was conducted in the respiratory medicine and pathology departments of a tertiary care teaching institute in West Bengal over a period of one year. One hundred-and-twenty patients presenting with thoracic mass lesions on chest radiograph and/or CT

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of the chest were included in this study. CT-guided FNAC was done in all the patients (n=120) and subsequently 88 of these underwent core needle biopsy and 12 underwent bronchoscopic biopsy.

We included patients aged 12 years and above of either sex presenting with intra-thoracic mass lesion (>30mm) on chest radiograph or CT. Patients with unstable cardiovascular status, acute myocardial infarction in last three months, any bleeding disorder and patients who did not give consent were excluded from the study. Approval of the Institutional Ethics Committee was obtained and a written informed consent was taken from every patient included in this study.

Detailed demographic and clinical parameters including smoking history, breathlessness, cough, weight loss, and haemoptysis were recorded. Laboratory investigations including complete blood count, sputum testing, chest radiography, and pulmonary function testing and contrast enhanced CT (CECT) of the thorax were done. For the subset of patients with bronchogenic carcinoma, ECOG performance status and clinical staging was done based on physical examination, CECT of thorax and abdomen and fiberoptic bronchoscopy and bronchoscopic biopsy was obtained in 12 patients.

A 21G spinal needle and 18G needle (core biopsy gun) were chosen for FNAC and core biopsy, respectively. Exact site and depth of needle entry were determined with the help of CT. Once the needle or core biopsy gun were inserted into the desired site, it was left for reference and a single axial scan was obtained to confirm the position of the needle followed by desired procedure. Air dried FNAC smears were stained by Leishman, Giemsa and Ziehl-Neelsen (ZN) stains. Alcohol fixed smear were stained with Papanicolaou and haematoxylin and eosin (H&E) stain for better visualisation of nucleus for the evaluation of malignancy. For demonstration of fungal structures, special stains such as periodic-acid Schiff (PAS) and Gomori's methenamine silver (GMS) were done in selected cases. After core needle biopsy and bronchoscopic biopsy, tissue was immediately put in 10% formal saline. Slides and tissues were sent to Pathology Department for cytological and histopathological evaluation along with relevant history and radiological findings. Immediately following the CT-guided procedures, one screening CT was done to look for the development of pneumothorax and a chest radiograph was obtained about an hour later to look for the delayed development of pneumothorax. The patients were monitored for other complications, if any, and were managed in the ward.

Statistical Analysis

If diagnosis obtained by cytology is same as the diagnosis obtained by biopsy, then we called it high concordance. So to find the concordance for adenocarcinoma, we took the numbers of cases diagnosed as adenocarcinoma by biopsy (B) and cytology (C) and divided B by C and calculated as percentage. Same was done for squamous cell carcinoma.

Comparisons were done using the Fisher's exact test and a p value <0.05 was considered to be statistically significant. Statistical analysis was performed using the Epi Info statistical software and Microsoft Excel.

Results

Of the 120 patients with intra-thoracic mass, 104 had lung mass and 16 had mediastinal mass (all were anterior mediastinal masses). CT-guided FNAC was done in all the cases (Figure 1 A&B) and subsequently core needle biopsies were done in 88 and bronchoscopic biopsies were done in 12. In 20 cases core needle biopsy was not done due to poor general condition (n=8), non-availability of consent (n=6) and high risk of pneumothorax due to the presence of gross emphysema (n=6). Their mean age was 52.8 years (range 12-83 years); 91 (75.8%) were males.

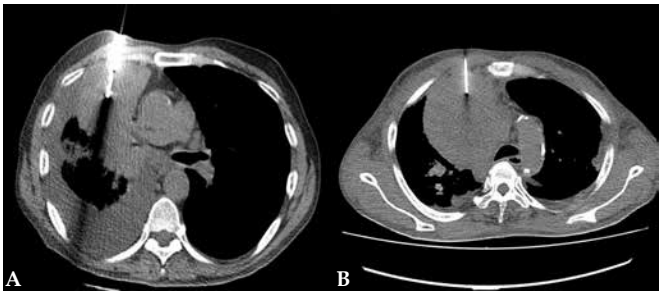

Figure 1. (A) Computed tomography-guided fine needle aspiration cytology (FNAC) showing peripherally located lung mass and (B) CT-guided core biopsy being done from a centrally located lung mass reaching up to the periphery.

Out of 120 CT-guided FNACs positive results were found in 110 patients with a diagnostic yield of 91.7%. Diagnostic yield for lung masses was 98/104 (94.2%) and for mediastinal masses was 12/16 (75%) (Table 1). Tuberculosis was the major infective aetiology presenting as thoracic mass (n=4) (Table 1). We had one case each of aspergilloma (Figure 2A) and hydatid cyst (Figure 2B) presenting as thoracic mass. The hydatid case was reported as inflammatory lesion in both CT-guided FNAC and biopsy but later on bronchoscopy, a whitish membrane was seen, which on biopsy showed features of a hydatid cyst.

The yield of CT-guided FNAC from mediastinal mass was 75% but yield was very high (100%) with CT-guided core needle biopsy. Thirteen out of 16 (81.3%) mediastinal masses turned out to be lymphoma. One case was diagnosed as benign teratoma and two cases were diagnosed as tuberculosis lymphadenitis.

Among the cases diagnosed as lymphoproliferative disease on CT-guided FNAC, 12 (75%) of them turned out to be non-Hodgkin's lymphoma (Figure 3A) and rest were Hodgkin's lymphoma (Figure 3B). Three of the six cases reported as "inflammatory" on FNAC, were diagnosed as cases of infective aetiology on biopsy. All cases reported as benign by FNAC were later proved to be benign on biopsy.

Table 1. Aetiological diagnosis

Diagnosis	No. (%)
Primary lung cancer	
Adenocarcinoma	44 (36.67)
Squamous cell carcinoma	38 (31.67)
Small cell carcinoma	6 (5.0)
Carcinoid	2 (1.7)
Other malignancies	
Plasmacytoma	1 (0.8)
Malignant teratoma	1 (0.8)
Pleomorphic sarcoma	1 (0.8)
Renal cell carcinoma metastases	1 (0.8)
Granulosa cell tumour	1 (0.8)
Lymphoma	16 (13.3)
Benign diagnosis	
Lipoma	1 (0.8)
Spindle cell tumour	1 (0.8)
Benign teratoma	1 (0.8)
Infective	
Tuberculosis	4 (3.3)
Aspergillosis	1 (0.8)
Lipoma	1 (0.8)

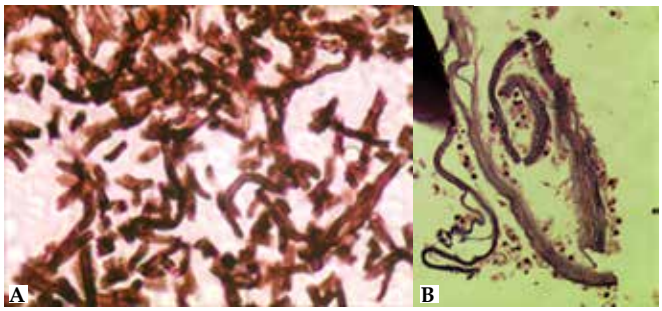

Figure 2. (A) Photomicrograph of computed tomography-guided fine needle aspiration cytology from a lung mass showing *Aspergillus hyphae* (Gomori methanamine silver × 200) and (B) photomicrograph of bronchoscopic biopsy specimen showing membrane of a hydatid cyst (Haematoxylin and eosin × 200).

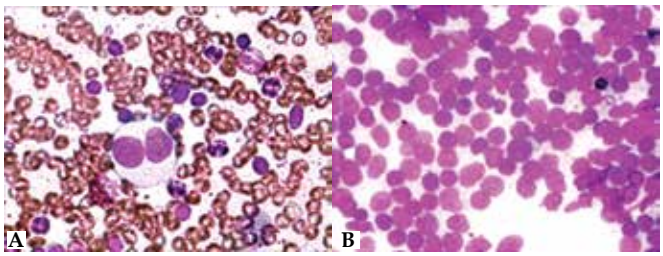

Figure 3. (A) Photomicrograph of CT-guided FNAC from the anterior mediastinal mass showing Reed Sternberg cell in a patient with Hodgkin's lymphoma (Leishman-Giemsa × 400) and (B) photomicrograph showing non-Hodgkin's lymphoma on (Leishman-Giemsa stain × 40).

Majority of the cases 64/110; (58.2%) diagnosed as lung cancer on FNAC were "suggestive" diagnosis, for example NSCLC suggestive of squamous cell carcinoma; NSCLC suggestive of adenocarcinoma; poorly-differentiated NSCLC or "suggestive of" lympho-proliferative disease. A complete diagnosis was possible in 94/100 (94%) on biopsy samples.

We observed a fairly good concordance between CT-guided FNAC and biopsy. Among the cases reported as adenocarcinoma, 90% proved to be adenocarcinoma (Figure 4A&B) (Table 2). Among the cases reported as suggestive of squamous cell carcinoma, 88.9% turned out to be squamous cell carcinoma (Figure 5A&B). All cases of small cell carcinoma were accurately diagnosed by CT-guided FNAC.

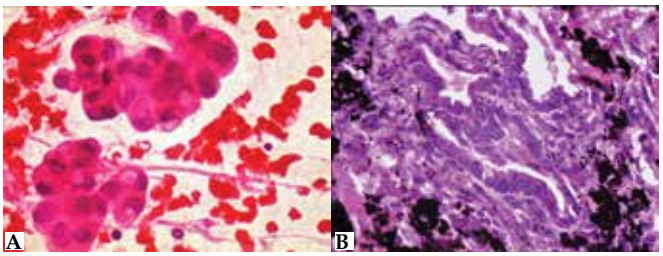

Figure 4. (A) Photomicrograph showing FNAC material from lung mass showing adenocarcinoma (Haematoxylin and eosin × 20) and (B) photomicrograph showing CT-guided core needle biopsy material from lung mass showing adenocarcinoma (Haematoxylin and eosin × 10).

Table 2. Cytolology and histopathology concordance for squamous cell carcinoma and adenocarcinoma

Suggestive Diagnosis on CT Guided FNAC		No.	Findings on Biopsy	
			Adeno	Squamous
NSCLC	Suggestive of squamous cell carcinoma	18	2	16
	Suggestive of adeno-carcinoma	20	18	2

Definition of abbreviations: CT=Computed tomography; FNAC=Fine needle aspiration cytology; NSCLC=Non-small cell lung cancer

Most of the patients with lung cancer in the present study were either smokers (39.3%) or ex-smokers (30.3%). Most of the females were non-smokers in this study. Squamous cell carcinoma was seen more commonly in male smokers, which was statistically significant. Association of smoking status and gender in relation to primary lung cancer is shown in the table 3. Lung cancer stages at presentation are shown in table 4. In the present study, 59.5% patients with NSCLC were in advanced stages (IIIB and IV stage) and rest of the patients were in early stages of the disease. Among the small cell carcinoma patients, five of the six patients came with extensive disease.

The ECOG stages of the primary lung cancer with respect to their stages of presentation are given in table 5. Most of the patients with lung cancer came with a poor performance status; 74% patients with primary lung cancer came with ECOG 3.

The complications after the diagnostic procedures are given in table 6. Pneumothorax was the most common complication arising out of CT-guided FNAC and biopsy. We found pneumothorax in 3/120 cases (2.5%) following CT-guided FNAC and in 8/88 cases (9.1%) following biopsy ($p<0.05$) (Figure 6). Chest tube placements were needed in six (5%) patients.

Table 3. Association of smoking status and gender in relation to primary lung cancer

Primary Lung Cancer	Male	Female	Smoker		Significant Difference Between Male and Female	Significant Difference Between Smoker and Non-smoker
			Male	Female		
Adenocarcinoma	31	13	23	10	P=0.29	P=0.79
Squamous cell carcinoma	35	3	34	1	P<0.005	P<0.005
Small cell carcinoma	4	2	4	0	–	–
Carcinoid	2	0	2	0	–	–

Table 4. Lung cancer stages at presentation

Type of Cancer	Non-small Cell Lung Carcinoma					Small Cell Carcinoma	
Stages	Stage I	Stage II	Stage IIIA	Stage IIIB	Stage IV	Limited Disease	Extensive Disease
Numbers (%)	1 (1.2)	7 (8.3)	26 (31.0)	24 (28.6)	26 (31.0)	1 (16.7)	5 (83.3)

Table 5. ECOG stages of the primary lung cancer with respect to their stages of presentation

Stage of Presentation of NSCLC and SCC	ECOG Performance Status			
	ECOG 1	ECOG 2	ECOG 3	ECOG 4
Upto Stage IIIA	3	8	20	1
Stage IIIB	0	1	22	1
Stage IV	0	0	21	5
SCC	0	0	4	3

Definition of abbreviations: ECOG=Eastern Cooperative Oncology Group; NSCLC=Non-small cell lung carcinoma; SCC=Small cell carcinoma

Table 6. Complications after the diagnostic procedures

Complications	FNAC	Biopsy	Bronchoscopy
Pneumothorax	3	8	0
Bleeding	0	2	2
Haemoptysis		1	2
Infection	0	1	0
Fever	0	2	4
Bronchospasm	0	0	3

Definition of abbreviation: FNAC=Fine needle aspiration cytology

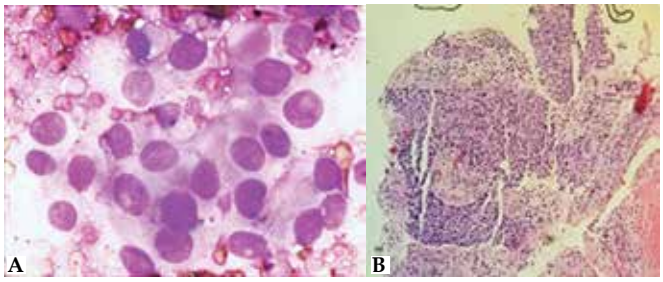

Figure 5. (A) Leishman Giemsa stain on CT guided FNAC material from a lung mass showing squamous cell carcinoma on 40x magnification; (B) Haematoxylin and eosin stain of bronchoscopic biopsy material showing squamous cell carcinoma on 4x magnification.

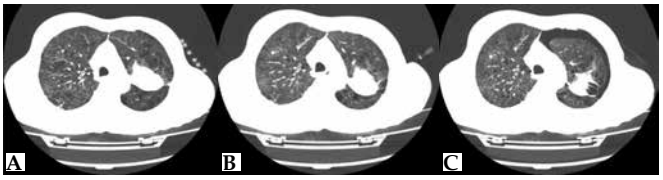

Figure 6. Development of pneumothorax after CT-guided FNAC; (A) determination of the site of needle insertion by placing radio-opaque material (needles) on the skin surface of the patient; (B) FNAC needle inserted to the desired site; and (C) development of pneumothorax seen after withdrawal of the FNAC needle.

Discussion

In the present study, 111 (92.5%) cases were found to be malignant by the various investigations. Benign neoplasms of the lung comprise less than one percent of all resected lung tumours.[1] We found 2.5% benign lesions presenting as thoracic mass. Among the malignant cases, 81.1% were primary lung cancers. Adenocarcinoma was the most common diagnosis in the study population. Various current studies[3,4] have also found adenocarcinoma to be the most common lung malignancy in patients with lung mass. Litzky[3] reported that adenocarcinoma to be the most common lung carcinoma in the United States. In another study,[4] the authors found 77.2% cases of intra-thoracic lesion to be primary malignancy. Earlier studies done in India reported also that adenocarcinoma is the most common lung carcinoma.[5,6] In another study,[6] adenocarcinoma was found to be the predominant cancer among both smokers and non-smokers.[6] We observed that squamous cell carcinoma was most common in male smokers (p<0.05).

Neyaz *et al*[7] found 3.7% cases of intra-thoracic mass to be tuberculosis, we found tuberculosis in 3.3% cases presenting as thoracic mass.

Kulkarni *et al*[8] in their study on core biopsy of mediastinal mass, found lymphoma to be the most common pathology presenting as mediastinal mass. We found mediastinal mass to be lymphoma in 13 (81.3%) patients in the present

study. On biopsy confirmation, 12 cases were found to be non-Hodgkin's lymphoma and four cases to be Hodgkin's lymphoma.

Cytopathological–histopathological concordance has been observed in 75% cases in one study.[9] We found concordance of 88.9% in squamous cell carcinoma and 90% for adenocarcinoma. Similar results were reported by others.[10,11]

For staging the lung cancer patients, we used the 7th edition of American Joint Committee on Cancer (AJCC) lung cancer staging system.[12] Noronha *et al*[7] reported that 43% of their patients with lung cancer were in stage III at presentation. In the present study, we found larger proportion of patients with later stage at presentation, which may be due to the fact that this study was done in a tertiary care centre and also due to lack of awareness among the general population and patient's low socio-economic status. Other several studies[13,14] have found that only 15% cases of lung cancer present at stage 1. In the present study, we found only one patient presenting in stage I. We observed that patients with later stage of malignancy (lung cancer) presented with poor performance status. Patients with lower stage than stage IIIA, presented with ECOG 2 or less. In the present study, 74% patients with primary lung cancer presented with ECOG 3. Most of the patients at later stage (stage IIIB and stage IV) presented with ECOG 3 or more. All patients with a diagnosis of squamous cell carcinoma presented with ECOG 3 or more; 34.3% patients presented with ECOG 2 or less who were diagnosed before or at stage IIIA.

In a large retrospective study of percutaneous lung biopsies,[16] incidence of pneumothorax was reported to be 20.5% and the incidence of pneumothorax requiring chest drainage was 3.1%. We found a lower rate of pneumothorax in both FNAC and biopsy. This difference may be due to the fact that most of the patients came at a very late stage of their disease and presented with a larger mass. We also observed that the risk of pneumothorax increases if the patient has diseased lung parenchyma, *e.g.,* emphysema. Earlier studies[17,18] have shown that most significant pneumothoraces will be detected on a chest radiograph performed one hour after the procedure, although these may not be visible on radiographs taken immediately after the procedure. We did one routine chest radiograph in the patients after one hour of the procedure to look for delayed pneumothorax. In our study, all pneumothoraces were detected in the routine CT screening done after the procedure.

In the present study, chest tubes were placed in 5% patients. Cox *et al*[19] found the pneumothorax rate to be 15% if non-aerated lung was traversed and approximately 50% if aerated lung was penetrated. Chest tube placement was needed in 25 (17.4%) of 144 cases of pneumothorax (7% of all biopsies).

Complication arising out of invasive procedures including bronchoscopy conducted for the assessment of mediastinal mass were similar to the observations reported in other studies.[8,20]

Conclusions

In the present study, adenocarcinoma was found to be the common primary lung cancer. We also observed high sensitivity of fine needle aspiration cytology in detecting malignancy with a high concordance with histopathology. We also found that patients with later stage of malignancy had poor performance status. In the present study pneumothorax was observed to be an infrequent complication of FNAC and biopsy.

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