

Computed tomogram guided fine-needle aspiration cytology of lung mass with histological correlation: A study in Eastern India

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Abstract

Background: Fine-needle aspiration cytology (FNAC) is an important and useful investigation, and is considered next to imaging in the rapid diagnosis of pulmonary mass lesion for the last few decades. **Aims:** To assess the role of Computed Tomogram (CT) guided FNAC in pulmonary mass lesions; to analyze the results; and to compare with histopathological findings.

Materials and Methods: The clinical, radiological, and cytological data of 130 patients were prospectively studied who underwent CT guided FNAC from October 2009 through September 2011. Thereafter these patients underwent bronchoscopic/trucut biopsy/lobectomy, whatever clinically indicated. Smears and tissue sections were evaluated simultaneously to reach at a definite diagnosis.

Results: Out of 130 cases, we found adequate FNAC smear and histopathology reports only in 124 cases. The age range varied from 35 to 73 years with the peak in the fifth to sixth decades. The benign lesions were 10 (8.07%) and malignant lesions were 114 (91.93%) shown by cytology. The most common tumor was adenocarcinoma (51.72%) followed by squamous cell carcinoma (22.41%) and small cell carcinoma 6.89%. Diagnostic accuracy of CT guided FNAC was 95%. Post procedural complications such as hemorrhage and chest pain were minimal and were noted only in three cases. **Conclusion:** CT guided FNAC of pulmonary masses provides simple, easy, and reliable method for reaching rapid tissue diagnosis with minimal complication.

Key words: FNAC, histological correlation, pulmonary mass

Introduction

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) scan. FNAC not only distinguishes between benign and malignant lesions but also helps in tumor typing of lung cancer, so initiation of specific therapy like chemotherapy or surgery is possible without unnecessary delay.

FNAC was first used by Martin and Ellis^[1] as a diagnostic tool. Leyden in 1883 and Menbriel in 1986 introduced the technique as diagnostic lung puncture for detection of malignancy and infections.^[2] More than three decades have passed, FNAC of pulmonary mass has gained worldwide momentum and acceptance, as it has further enhanced the diagnostic usefulness of clinical cytology in lung and mediastinal cancer diagnosis.^[3] FNAC has long been used for the non-surgical confirmation of primary as well as metastatic thoracic lesions. The special advantage of FNAC includes detection of those tumor types like small cell carcinoma, lymphomas more appropriately

treated by chemotherapy rather than surgery. Numerous literatures supported that CT-guided FNAC is an accurate and sensitive way of diagnosing malignancy of the thorax.^[4,5] This procedure is almost minimum painful non-operative procedure as compared with biopsy for diagnosis of pulmonary mass, outweighs the single major rare complication of pneumothorax.^[5]

The present study was undertaken to know the pathological spectrum of pulmonary lesions; to correlate cytological findings with histological features; and to assess the accuracy of FNAC in evaluation of lung masses.

Materials and Methods

The study was conducted in the department of Pathology, in our medical college and hospital, during the period of Sep 2009 - Aug 2011. There were consecutive cases over a period of two years. One hundred and thirty (130) patients having pulmonary mass lesions suspected to be neoplastic by chest radiograph and/or CT scan were referred from different departments like chest, medicine, and oncology. One hundred and twenty four (124) cases were included in this prospective study as cytological examination showed an inadequate cell in six cases. This prospective study was approved by the hospital ethics committee.

CT guided FNAC of pulmonary mass lesions from each case were performed by our senior pathologist as OPD procedure and also in presence of experienced radiologist after explaining the risks and benefits. From each patient, informed consent was taken. The skin surface was cleaned with povidone iodine, and then 21 G-88 mm long spinal needle was introduced through percutaneous/transsthoracic approach localizing the exact position by CT scan after the measurement of the site and angle of entry of the needle,

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route of the needle, and the distance between the skin and lesion on the CT scan monitor.^[6] Following placement of the needle, a CT scan slice was taken to ascertain whether the tip of the needle was within the mass. The aspirate was obtained by to and fro and rotating movements of the needle within the lesions and five smears were prepared immediately from the sample in the CT scan room. Air-dried smears were stained with Leishman-Giemsa (L and G) stain, whereas alcohol-fixed smears were stained with Papanicolaou (PAP) stain for rapid cytopathological evaluation of the lesions.

Patients were kept for 2 hours under observation. In our study, mild hemorrhage from peri-lesional area in one case and chest pain in two cases was found, which could be managed conservatively. We exclude those cases that were suffering from severe

Chronic obstructive pulmonary disease (COPD), bleeding disorders, pulmonary arterial hypertension (PAH) and contra lateral pneumonectomy cases and that were unable to hold breath.^[6]

Subsequently biopsy (bronchoscopic/trucut biopsy) or lobectomy specimens were then examined in pathology department for histopathological examination (HPE). The sections were stained with routine hematoxyline and eosin (H and E) stain, examined under light microscope. Immune-histochemistry was done in few cases, where necessary.

After data collection, they were tabulated and analysis was done with use of Med cal C software.

Result and Analysis

A total of 124 cases were included in the study where

Table 1: Demographic description of the study

Subject	Total No.	Percentage
Age	4	3.22
<40 yrs	16	12.9
40-49 yrs	60	48.38
50-59 yrs	40	32.28
60-69 yrs	4	3.22
70 yrs and above		
Sex	80	64.51
Male	44	35.49
Female		
Side of lesion		
Right	72	58.06
Left	52	41.94
History of smoking		
Smoker	70	56.45
Non smoker	54	43.55
Provisional diagnosis by CT scan/chest X ray		
Benign	6	4.83
Malignant	118	95.17
Cytological diagnosis		
Benign	10	8.07
Malignant	114	91.93
Histological diagnosis		
Benign	09	7.25
Malignant	115	92.75

we got both adequate FNAC smear and histopathology report of thoracic masses. Out of 124 cases, 80 cases (64.51%) were male and 44 (35.49%) were female. General demographic findings of the study and common disease pattern have been given in Table 1. In our study, cytological diagnosis showed maximum number of cases belonged to adenocarcinoma (48%). The other diseases spectrum were squamous cell carcinoma (21%), small cell carcinoma (13%), carcinoid (5%), nonspecific inflammation (4%), large cell carcinoma (2%), benign cystic lesion (2%), granulomatous inflammation (2%), dermoid (1%), spindle cell neoplasm (1%), and bronchiolo-alveolar carcinoma (1%). There were four cases below 40 years of age. Majority of the cases were seen in fifth and sixth decade. Cytological examination showed that 114 cases were malignant and 10 cases were benign. Provisional diagnosis based as radiologic findings were 116 cases malignant and 8 cases benign. The diagnostic sensitivity of FNAC for bronchogenic carcinoma was 97% and specificity was 90%, positive predictive value 99%, negative predictive value 77%. The diagnostic accuracy of CT guided FNAC was 95% based on final HPE report.

In our study, a total of 114 malignant cases were detected by FNAC. Among the malignant lesions, most common carcinoma [Table 2] was adenocarcinoma 60 (52.63%) followed by squamous cell carcinoma 26 (22.8%), among malignant lesions. There was male preponderance in both adenocarcinoma (2:1) and squamous cell carcinoma (5:1). Smokers were most common (69%) among squamous cell carcinoma cases.

FNAC showed that 114 cases were malignant and 10 cases were benign. Whereas HPE revealed 115 cases were malignant and 9 cases were benign. All cytological diagnoses were correlated with histological diagnoses [Table 3]. In few cases like carcinoid and spindle cell neoplasm (MPNST) we used Immuno histo-chemistry (IHC) i.e., chromogranin A, cytokeratin, and S-100 for confirmation of diagnosis. We found discordances regarding 3 benign and 3 malignant lesions.

Benign lesion

One lesion diagnosed as nonspecific inflammation by FNAC, finally that case was diagnosed by HPE as squamous cell carcinoma with secondary inflammation. The other two cases diagnosed by FNAC as benign cystic lesion and granulomatous inflammation turned out to be a Hydatid cyst and Aspergillosis [Figure 1a and b], respectively, after HPE.

Malignant lesions

Microscopically, most adenocarcinomas [Figure 1c and d], squamous cell carcinomas [Figure 2a], and small cell carcinomas [Figure 2b] showed classical cytomorphological features. In our study, we found six cases of carcinoid tumor [Figure 3], two cases of bronchiolo-alveolar carcinoma [Figure 2c and d], two cases of large cell anaplastic and one case of spindle cell neoplasm, which was finally diagnosed as

Table 2: Distribution of malignant lesions according to sex and smoking habit

Malignant lesions (by FNAC)	Male		Female		Smoker		Non smoker	
	No	%	No	%	No	%	No	%
Adenocarcinoma 52.63% (n=60)	40	67	20	33	32	53	28	47
Squamous cell carcinoma 22.8% (n=26)	20	77	6	23	18	69	08	31
Small cell carcinoma 14.91% (n=17)	9	53	8	47	10	58.8	07	41.2
Carcinoid 5.29% (n=6)	4	67	2	33	4	67	2	33
Bronchiolo-alveolar carcinoma 1.75% (n=2)	2	100	Nil		2	100	Nil	
Large cell anaplastic carcinoma 1.75% (n=2)	2	100	Nil		2	100	Nil	
Spindle cell neoplasm 0.87% (n=1)	1	100	Nil		1	100	Nil	
Total=114	78		36		69		45	

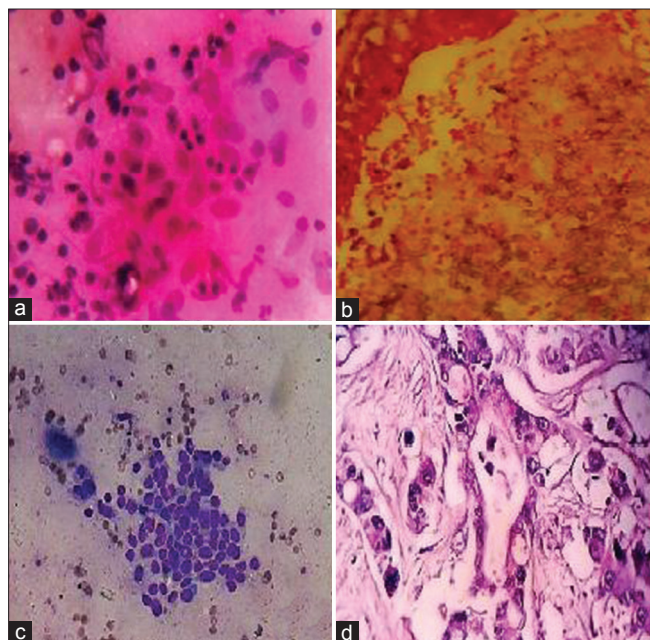


Figure 1: (a) Cytology smear showing ill formed granulomas (Leishman and Giemsa stain, x400), (b) Biopsy showing fungal colony of *Aspergillus* (Hematoxyline and Eosin stain, x400), (c) Cytology smear showing cluster of epithelial cell arranged in acini. The cells have prominent nucleoli (Leishman and Giemsa stain, x100), (d) Histology section of lung mass showing well differentiated adenocarcinoma (Hematoxyline and Eosin stain, x400)

malignant peripheral nerve sheath tumor (MPNST) by HPE as well as proved by immuno histochemistry (S-100 positive).

One case diagnosed as squamous cell carcinoma by FNAC but HPE showed chronic nonspecific inflammation with focal squamous metaplasia of lining respiratory epithelium. The other two cases FNAC marked as adenocarcinoma but HPE revealed those as poorly differentiated squamous cell carcinoma [Table 3].

In our study, HPE reports of pulmonary tumors were considered as final confirmatory report. So correlation was established between CT guided FNAC findings and provisional diagnosis by radiology by calculating weighted Kappa value. The weighted Kappa values were 0.816, 0.602, and 95% confidence interval were (0.64 to 0.99) and (0.39 to 0.86) for CT guided FNAC reports and radiological diagnosis, respectively. It was found that CT guided FNAC diagnosis showed almost perfect agreement, whereas radiological

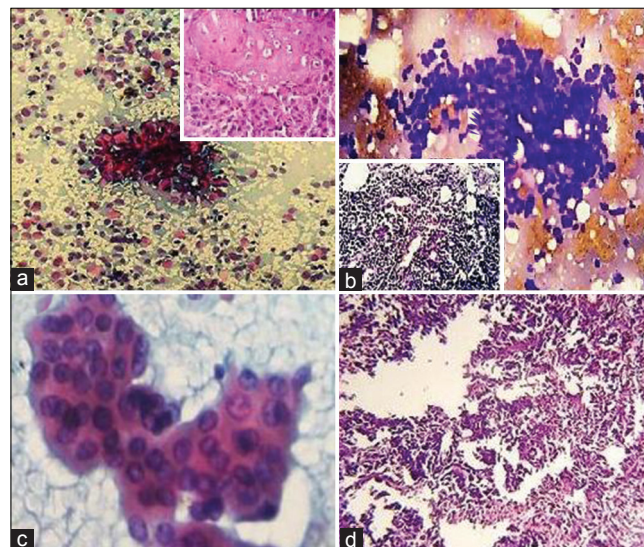


Figure 2: (a) Squamous cell carcinoma, Cytologic smear showing malignant squamous cells in clusters and dispersed singly (PAP stain x400), Histologic section showed (inset) malignant squamous cell in sheets with keratin pearl formation (Hematoxyline and Eosin stain, x400), (b) Small cell carcinoma, Cytologic smears showing – small sized cells in tight groups showing nuclear molding, coarse clumped chromatin (Leishman and Giemsa stain, x100), Histologic section showed (inset)-small cells with dark hyper chromatic nuclei, atypical mitosis, areas of necrosis, (Haematoxyline and Eosin stain, x200), (c) Bronchiolo-alveolar carcinoma, Smear showed round to oval uniform cells in monolayer sheet with high nuclear cytoplasmic ratio and intra nuclear groove. (Leishman and Giemsa stain, x400), (d) Bronchiolo-alveolar carcinoma, Histologic section showing lepidic pattern of growth ((Hematoxyline and Eosin stain, x100)

diagnosis showed moderate agreement with HPE diagnosis.

Discussion

FNAC is an accurate and safe method for evaluation of pulmonary mass. It enables categorization of malignant lesions in the vast majority of cases. It is also useful in diagnosis of dermoid. In our present study, 124 FNAC from pulmonary mass lesions were evaluated over a period of two years, all cases showed adequate cells in FNA smear as well as subsequently was performed irrespective of clinical diagnosis.

All cases enrolled were adults. The peak age of incidence (50-59 years) was the same as that documented in recent studies.^[2,7] Of these cases, 10 (8.07%) were benign and 114 (91.93%) were malignant as per FNAC findings. The reason may be due to increased incidence of malignancy

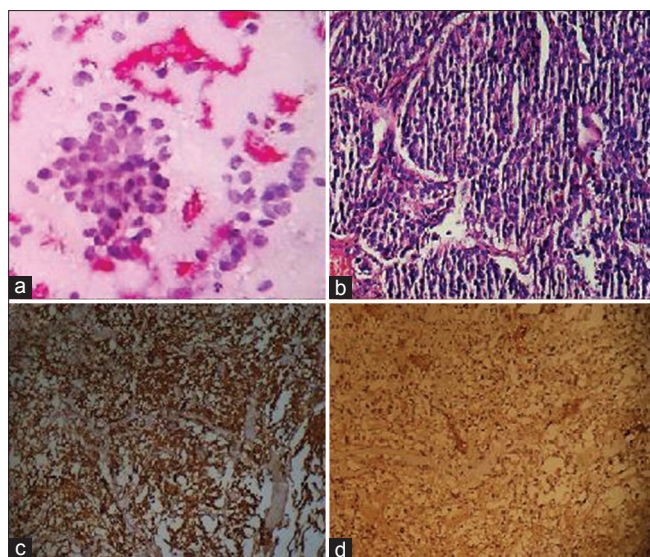


Figure 3: Carcinoid Tumor (a) Cytology smears showing monomorphic population of small round cells with stippled chromatin (Leishman and Giemsa stain, x400), (b) Histologic section showed uniform round cells forming nests and rosettes (Hematoxyline and Eosin stain, x100), (c) Immuno-histochemistry showed tumor cells positive for Chromogranin A positive, (d) Immuno-histochemistry showed tumor cells negative for Cytokeratin – negative

Table 3: Cytological and histopathological correlation

Cytological diagnosis	Number	Correlation	Concordant	Discordant
Benign				
Nonspecific inflammation	5	5	4	1
Dermoid	1	1	1	
Benign cystic lesion	2	2	1	1
Granulomatous inflammation	2	2	1	1
Malignant				
Carcinoma	105	105	103	3
Carcinoid	6	6	6	
Sarcoma	1	1	1	

in this age group as FNAC was mainly used for diagnosis for neoplasm. But HPE showed 9 (7.25%) cases were benign and 115 (92.75%) cases were malignant. The mean age in our study was 56.6 years, which is almost similar with (56.4 years) and (56.8 years) to studies conducted by Singh *et al.*,^[8] and Saha *et al.*,^[7] respectively. Power *et al.*,^[9] also showed increased prevalence of thoracic neoplasm after the age of 50 years, with an average age of 54 years.

There was male preponderance (64.51%) in our study compared to female. The percentage of male patients was a little higher in our series than in three recent studies i.e., 71.1%,^[10] 78.9%^[7], and 80.6%^[11], respectively.

In this study, lung tumors were located more on the right side than on the left. Among the patients, 56.45% were active smokers. Cytological diagnosis was made in 124 out of 130 cases (95.38%) and the high incidence of malignancy (91.93%) was comparable with that found in other studies.

[7,11,12] The malignant cases formed largest category including carcinoma, neuroendocrine tumors, and sarcoma. Among all 114 cases of malignant pulmonary tumors, the most common ($n = 60$; 52.63%) was adenocarcinoma followed by 22.8% squamous cell carcinoma, and 14% small cell carcinoma. The incidence of adenocarcinoma was reported to be significantly higher than that of squamous cell carcinoma in recent studies by Tan *et al.*,^[10] and Madan *et al.*,^[13] Whereas in certain other national and international studies, prevalence of squamous cell carcinoma was more than adenocarcinoma.^[2, 11,14-16] In Our study we found 1% case of bronchiolo-alveolar carcinoma (BAC). There is change in concept regarding diagnosis of BAC. Travis *et al.*,^[17] in 2011 recommended discontinuing the term 'BAC' (strong recommendation, low quality evidence). For small (≤ 3 cm) solitary adenocarcinoma with pure lepidic growth, they recommended the term adenocarcinoma *in situ* (AIS). For same size and same pattern of growth with small foci of invasion ≤ 0.5 cm-a new concept of minimally invasive carcinoma (MIA) to be considered. But AIS or MIA should not be used in small biopsy or cytology specimen. So, BAC can be regarded as an adenocarcinoma with lepidic growth with or without invasion. But in our study, we followed the earlier classification of lung tumors and BAC was included one of the entities.

The efficacy of CT guided FNAC in the diagnosis of benign and malignant lesion was 67% versus 97%. It is evident from the Table 2, adenocarcinoma, squamous cell carcinoma; small cell carcinoma, neuroendocrine carcinoma can be effectively diagnosed by cytology. A high degree of accuracy in cytological typing can be of great importance in those cases where no confirmatory histology is available. Maximum cases of lung malignancy were primary while only one case of represented as metastatic adenocarcinoma of prostate.

Though pneumothorax was most common complication of other studies, but we did not found any case in our study. The overall rate of complications (2.4%) in our study was also remarkably less than other series where the range varied from 6 to 50%.^[10,11] In our study, mild hemorrhage from perilesional area in one case and chest pain in two cases was found and which could be managed conservatively.

In our study, CT guided FNAC showed almost perfect agreement with histological diagnosis in comparison to radiological opinion. So FNAC was found to be highly accurate (95%) in diagnosis of lung mass as almost similar shown by previous studies.^[13,14] Hence CT guided FNAC diagnosis alone can be used with confidence to select treatment modalities and to avoid unnecessary surgeries in patients with lung malignancies.

Conclusion

CT guided FNAC is a simple, safe, and reliable procedure with high diagnostic accuracy for the diagnosis and sub typing of lung cancer. Though complications are rare, peri-lesional hemorrhage, and chest pain are occasionally encountered, but rarely require active management.

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