Original Article

Indian Journal of Pathology: Research and Practice
Volume 6 Number 1, January - March 2017
DOI: http://dx.doi.org/10.21088/ijprp.2278.148X.6117.20

Role of FNAC Using Imaging Techniques in Diagnosing the Lung Lesions

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Abstract

Background and Objectives: FNAC play a vital role in evaluating pulmonary lesion. Its diagnostic accuracy is high in diagnosing lung cancer. From therapeutic view it is essential to categorize small cell lung carcinoma(SCLC) from Non small cell lung carcinoma. However recent targeted therapy emphasizes classification of NSCLC into different categories like squamous cell carcinoma(SQC), adenocarcinoma(AC) and Poorly differentiated carcinoma(PDC). The present study highlights utility of FNAC in diagnosing and categorizing lung cancer into various groups on which patient management is based. *Materials and Methods:* Present study is a prospective descriptive study. A total 25 FNAC of lung lesions under therapeutic guidance were included in the study. FNA smears were further stained and detailed cytomorphological study was done. Cytological parameters which were were studied include cellularity, cell arrangement, cell morphology and background material. *Results:* Mean age of the patients was 60.08years, 88% were males and 12% were females. Imaging technique used in 88% cases was ultrasonography and in 12% cases CT was used. In 8% cases aspirate was inadequate to comment. FNA diagnosis in 80% cases was positive for malignancy. Among malignant cases 35% were adenocarcinoma, 30% were squamous cell carcinoma, 25% were poorly differentiated carcinoma and 10% cases were metastasis. *Conclusion:* FNA is highly reliable method in not only distinguishing SCLC from NSCLC, but also categorizes NSCLC into SQC, AC and with the help of ancillary techniques one could even know the line of differentiation of PDC which really helps in patient management.

Keywords: Squamous Cell Carcinoma; Lung Cancer; Adenocarcinoma; Small Cell Carcinoma.

Introduction

Pulmonary nodules discovered by a imaging technique presents a relatively frequent clinical problem. However, in nodules larger than 2cms, the incidence of primary lung cancer ranges from 64-82% [1]. An early accurate diagnosis is of paramount importance for initiating specific therapy for malignant lesions. Thus after clinical risk assessment tissue diagnosis is the next step in managing radiologically suspicious nodules. Direct tissue sampling for diagnosis is essential in most patients for decisions regarding treatment and can be accomplished by fine needle aspiration biopsy (FNAB), endoscopic or core needle biopsy or surgical resection. Sampling of the lesion by FNAB can be performed via airway(endobronchialtransbronchial FNAB) or chest wall(USG/CT guided percutaneous FNAB) [2]. FNAB has become recognized as asafe and effective diagnostic tool, as a result of improved aspiration biopsy tools and techniques, better control of complications and increased experience of cytopathologists in interpreting aspiration specimens. New developments in the field of thoracic oncology have challenged the way pathologists approach the diagnosis of pulmonary carcinoma. From a therapeutic standpoint lung cancer should be cytologically divided into small cell carcinoma(SCC) and non small cell carcinoma(NSCC) [3]. NSCC is no longer an adequate diagnostic category. Pathologists are required to further classify tumors into adenocarcinoma and squamous cell carcinoma since specific therapies are now recommended depending on the histological tumor type. The vast majority of

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(**Received on** 15.12.2016, **Accepted on** 23.12.2016)

lung cancer is diagnosed in advanced clinical stages wherecytologic or small biopsy material is the only form of tissue diagnosis, thus placing cytology especially FNAB in the front line for management of lung cancer. In the present study we highlight cytological classification and cytomorphological aspects of lung cancer with review on ancillary techniques used with FNAC.

Material and Methods

The present study is a prospective study done over a period two years from January 2015 to November 2016.A total of twenty fivepatients presenting with lung lesion on plain X-ray were included in the study. All such eligible patients underwent FNAC using imaging techniques like Ultrasonographic guidance or CT guidance as per the standard guidelines after obtaining an informed consent. Most patients required three or fewer passes for an adequate specimen. The aspirates were smeared onto glass slides and then fixed in alcohol fixative. Staining is done with routine Hematoxylin and eosin stain. These smears were examined in cytology department by the reporting pathologist. All the clinical and radiological details were collected from the patient records. The samples were assessed for adequacy, considered adequate when they are rich in cellularity. On the contrary , they were considered inadequate when cellularity was poor or absent and in case of necrosis, hematic or perilesional material. Detailed cytomorphological study was done. Cytomorphological aspects which were assessed include adequacy, if adequate following parameters were analyzed:cellularity, cell arrangement, cell morphology (Cytoplasmic and nuclear Pleomorphism, chromatin distribution, nucleoli, intranuclear inclusions, bizarre cells, giant cells), background material(looked for keratinous/ mucinous/ necrotic/ myxoid material) . The lesions were classified as positive for malignancy or negative for malignancy. If positive for malignancy tumors were classified SCC(Small cell carcinoma) and NSCC (Non small cell carcinoma). NSCC was further classified as adenocarcinoma, squamous cell carcinoma and poorly differentiated carcinoma. However histopathological correlation was not possible, as these patients were referred for higher center. If negative for malignancy they were either acute inflammatory/ chronic inflammatory lesion.

Results

During the study period USG/CT guided FNAC of lung lesions was done on 25patients. Indication for guided FNAC was nodule in the lung on chest X ray. In 44%(n=11) cases nodule was in right lung, in 52%(n=13) cases the nodule was in left lung and in 4%(n=1) nodules were in bilateral lung fields. The referral department was oncology in 76%(n=19) cases, surgery in 20%(n=5)cases and medicine in 4%(n=1)cases. Mean age of the patients was 60.08 years. Males were 88% and females were 12%.

Table 1: Distribution of cases based on FNA diagnosis

FNA Diagnosis	Number of cases	Percentage
Acute inflammation	2	8%
Granulomatous inflammation	1	4%
Positive for malignancy	20	80%
Inadequate for interpretation	2	8%
	25	100

Table 2: Cytological subtyping of malignant cases

Malignancy –Typing	Number	Percentage
A)Non small cell carcinoma		
1)Adenocarcinoma	7	28%
-Conventional	6	24%
-Bronchoalveolar carcinoma	1	4%
2)Squamous cell carcinoma	6	24%
3)Poorly differentiated carcinoma	5	20%
B)Small cell carcinoma	Nil	Nil
C)Metastasis / secondaries	2	8%
	20	80%

Diagnostic accuracy was 92% considering the cytological criteria as the standard. Most common cytological finding was malignancy in 80% of the cases followed by inflammation in 12% cases. It was acute suppurative/pyogenic inflammation in 4% cases, acute suppurative secondary to fungal in 4% cases and granulomatous inflammation suggestive of tuberculosis in 4% cases. FNA aspirate was adequate

to make the diagnosis in 92% cases and inadequate in 8% cases. Inadequacy was due to hemorrhagic aspirate which showed only cellular components of blood.

Distinction of a malignant process from non-neoplastic process in specimens that are suboptimal for evaluation / reactive squamous atypia/ reactive type II pneumocytes can be extremely difficult and an unequivocal diagnosis shold be rendered only in aspirates with adequate tissue. Clinical and radiological correlation to ensure accurate diagnosis in such setting is of utmost importance.

Out of twenty FNAC proven cases of malignancy, most common malignant tumor was adenocarcinoma (28%) followed by squamous cell carcinoma(24%). One case was bronchoalveolarcarcinoma(4%) which was categorized under adenocarcinoma showed classical cytological features. Poorly differentiated carcinoma were 20% which showed features of epithelial malignancy without any differentiation, hence adviced histopathology for typing. Secondaries were 8% which showed cytological features of sarcoma and typed as chondrosarcoma with primary in ribs and fibrosarcoma with primary in thigh.

Table 3: Cytological criterias used to subtype malignancy [4,5,6]

Malignant Subtyping	Cytological Features
A)Non small cell carcinoma	
-Adenocarcinoma	
Conventional	Smears are cellular with papillary, acinar, cell ball and 3 dimensional cell clusters. Individual cells are round/cuboidal/columnar with vacuolated cytoplasm and vague cell border. Nuclei exhibit open chromatin with prominent nucleoli. Mucin is present
Bronchoalveolar carcinoma	Non mucinous type-Smears are cellular with large cohesive monolayered sheets of cuboidal to dome shaped epithelial cells with fine chromatin, pinpoint nucleoli and fine cytoplasmic vesicles .
	Mucinous type- Glands with basally placed nuclei and clear to orangeophilic columnar cytoplasm with luminar margins. The nuclei have evenly dispersed chromatin, nuclear grooves and pinpoint nucleoli.
-Squamous cell carcinoma	Smears are cellular with large sheets and cohesive clusters. Individual cells are polygonal/ spindled/ tad pole with dense cytoplasm and distinct cell border. Nuclei exhibit coarse chromatin, micronucleoli. Presence of keratin.
-Poorly differentiated Carcinoma	Smears are cellular with 3 dimensional cell clusters and discohesive tumor cells. These cells show high N/C ratio, nuclear pleomorphism and variable chromatin and prominent nucleoli.Immunohistochemistry(IHC) is useful in characteriing the line of differentiation as adenocarcinoma versus squamous cell carcinoma . IHC markers include TTF1, Napsin A, CK 5/6, P63.
-Large cell(Neuroendocrine carcinoma)	Smears are cellular, cells are pleomorphic with abundant cytoplasm and contain nuclei with fine chromatin and prominent nucleoli. However IHC is needed for confirmation.
B)Small cell carcinoma	Smears are cellular , abundant single and loosely cohesive groups . Cells are small, monotonus with round to spindled shape and demonstrate nuclear molding. They have high N/C ratio, scant cytoplasm, homogenous fine chromatin. Nucleoli are absent/inconspicuous. Apototic cells, single cell necrosis and mitotic figures are frequent.

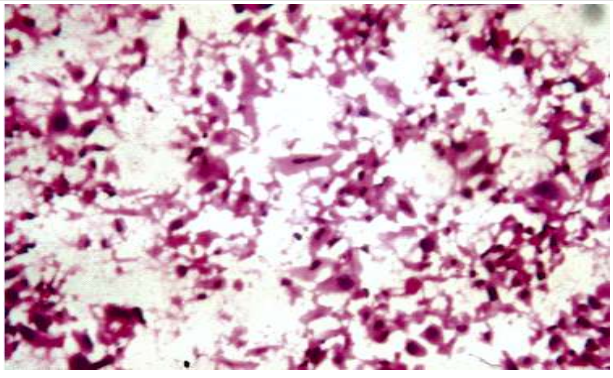

Fig. 1: Squamous cell carcinoma – lung, showing cells with abundant dense cytoplasm, well defined cell bordes. There is nuclear pleomorphism, coarse chromatin and binucleation.

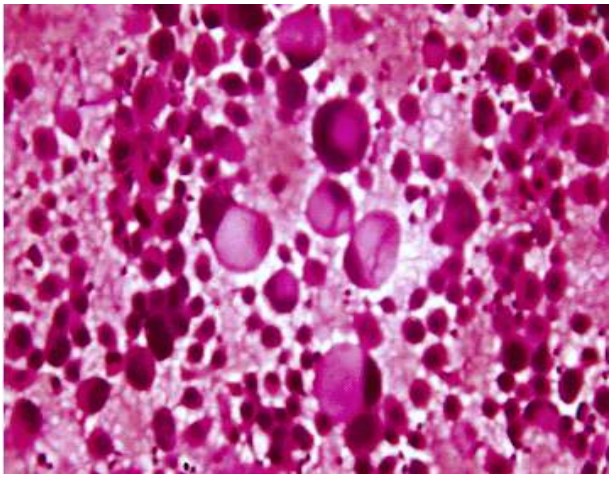

Fig. 2: Adenocarcinoma –Signet ring variant, Showing cells with abundant mucinous cytoplasm and peripheral pushed hyperchromatic nucleus

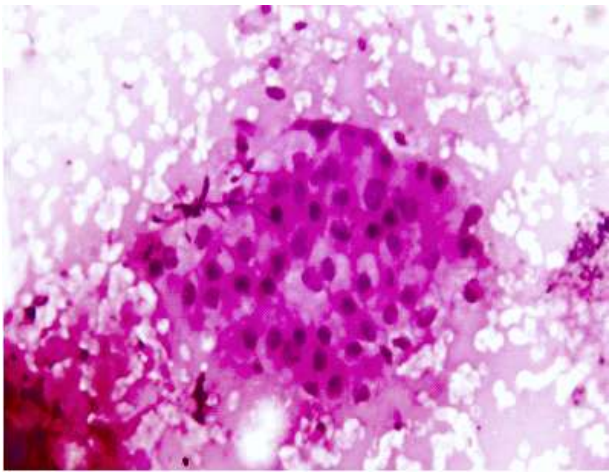

Fig. 3: BAC –Broncho alveolar carcinoma showing monolayered sheets of cells with foamycytoplasm andmoderate nuclear pleomorphism

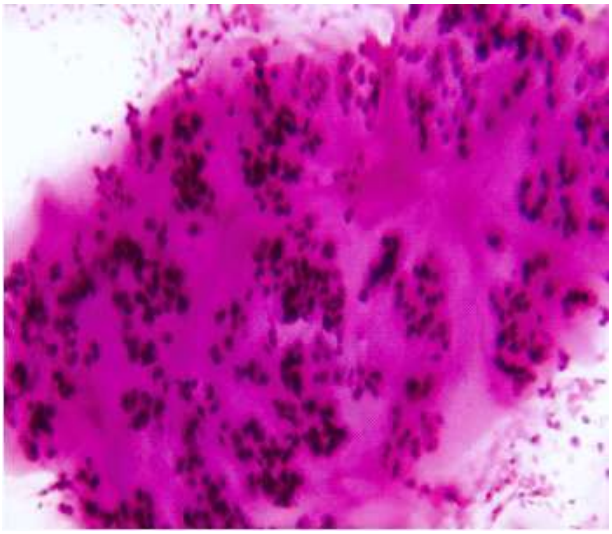

Fig. 4: Metastatic chondrosarcoma showing chondrocytes with nuclear atypia in the background of chondromyxoidstroma

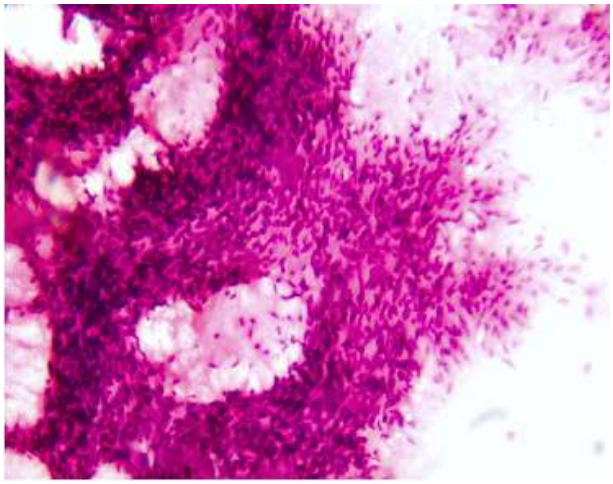

Fig. 5: Metastatic fibrosarcoma showing spindle cell tissue fragment composed of spindle cells with nuclear atypia and hyperchromatisim.

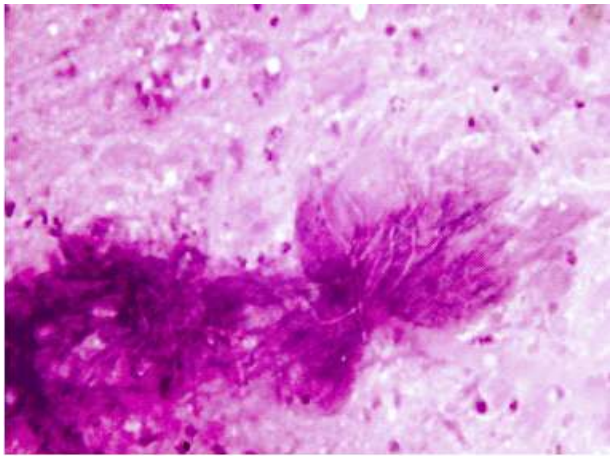

Fig. 6: Inflammatory process secondary to funus showing septate translucent hyphae in the background of necrosis

Discussion

The use of lung cytology has evolved in the last few years. Emphasis has shifted from diagnosis of malignancy and confirmation of metastatic tumors to its use as a definitive diagnostic procedures on which patient management decisions are based [7]. The oldest and most fundamental cytological method was based on sputum cytology this was followed by bronchoscopic techniques like bronchial washings, bronchial brushing and bronchoalveolarlavage, the final frontier for obtaining adequate material is FNAC [8]. If lung cytology is to be used for diagnosis and prognostication its sensitivity and specificity need to be high. Of all the cytological procedures FNAC has been proved to be the most accurate tool in diagnosis of lung carcinoma. Compared to conventional respiratory cytology the incidence of complication is low. Two basic factors influence clinical management

of lung cancer is a)The stage of the disease at the time of diagnosis assessed clinically and radiologically b)Tumor type as evaluated by the pathologist.

The intrinsic advantages of FNAC are safety, minimal trauma to patients, rapidity, cost effective and also ancillary techniques can be applied to material collected by FNAC. The advances in the understanding of molecular mechanisms underlying lung cancer and development of new targeted therapies challenge the traditional dichotomization between Small cell lung carcinoma (SCLC) and Non small cell lung carcinoma (NSCLC) and prompt a more specific categorization of NSCLC into squamous cell carcinoma(SQC) or adenocarcinoma(AC).

Published reports reveal that sensitivity of FNAB for diagnosis of lung cancer ranges from 56-90% where as specificity is close to 100%. In nearly all these studies [9,10] false positive rate is less than 1% and false negative rate of around 10%. The major contribution of relatively high false negative rate is failure to obtain diagnostic material most commonly due to sampling error. In the present study diagnosis was not possible in 8% of the cases and the smears showed scant to no cellularity in the hemorrhagic background.

Table 4: Comparison of rate of inadequacy/ unsatisifactory specimen in various studies

Studies	Inadequacy(%age)
Stewart et al[11]	2.7
Crosby et al[12]	16
Alanso et al[13]	17
Tiao et al[14]	8
Present study	8

Stewart et al found low rates of inadequacy ,since they followed immediate cytology assessment which include requirement of cytopathologist in or close to radiology department . After FNA immediately one/ two smear are stained with Diff quick and assessed for cellularity. If the first aspirate was considered doubtful a second FNA was requested thus reducing inadequacy rate. On site adequacy evaluation also provides real time communication information including appropriate tissue triage recommended for ancillary tests such as molecular testing, flow cytometry, cytogenetics, electron microscopy and so forth. Thus interaction directly impacts on clinical management.

In the present study there was male preponderance which is similar to other studies [15]. This male preponderance is explained on the higher incidence of predisposing factors like smoking, COPD and alcoholism in males. Mean age on the patients was 60 years. Imaging technique used in 88% cases was ultrasonography and in 12% cases CT was used.Indication for guided FNAC was lesion/mass in the lung, in 44% cases the mass was in right lung, 52% cases the mass was in left lung and in 4% cases the lesion was in bilateral lung fields.

FNA diagnosis in 80% cases was positive for malignancy, in 12% cases it was negative for malignancy and in 8% cases aspirate was inadequate to comment. Out of 80% malignant diagnosis – 35% cases were adenocarcinoma, 30% cases were squamous cell carcinoma, 25% were poorly differentiated carcinoma and 10% cases were metastasis - malingnant spindle cell lesion S/O sarcoma. 12% cases were negative for malignancy out of which acute suppurative inflammation formed 8% cases and chronic granulomatous inflammation formed 4% cases.

In the present study small cell carcinoma(SCLC) was not found due to small sample size and rarity of of SCLC with incidence of 5-7% [3] and cytology is highly accurate and well recognized to distinguishSCLC from NSCLC, in a study of 259 consecutive lung FNAC by Delgado et al [3] SCLC was distinguished from NSCLC with accuracy of 96%. From the therapeutic standpoint it is very important to distinguish SCLC from NSCLC. Classical morphological features of SCLC such as nuclear molding, frequent mitoses and absence of nucleoli are often distorted on small surgical biopsy with extensive crush artifact. In this setting cytology has edge over histology because of better preservation and fewer artefacts [16].

Based on recent studies cytology provides several advantages over surgical speciments for subtyping of NSCLC [17]. The key morphological criteria for adenocarcinoma(AC) versus SQC are gland versus keratin respectively. In the present study AC were more common followed by SQC and poorly differentiated carcinoma(PDC). The Papanicolaou stain has exquisite sensitivity for even minimal keratinization aiding in distinction of SQC from AC. The morphological patterns which emerge in tumor smears provide a clue to a tumor subtype which may not apparent in surgical specimens. In addition due to immediate fixation cytology provides greater nuclear and cytoplasmic resolution than histology . While in majority of cases a line of differentiation can be clearly identified by morphology, difficulty arises in subset of cases.

Difficulties encountered in the interpretation and accurate classification of NSCLC were poor differentiation of the tumor where distinguishing morphological features are not apparent followed by scant cellularity. Non keratinizing poorly

differentiated SQC in particular is subject to misclassification by FNAB. Another difficulty is presented by tumors with mixed histology but true adenosquamous cell carcinoma are infrequent with reported incidence of 2-3% in publication series [18,19].

Despite these limitations using cytomorphology and immunocytochemistry one can subclassify NSCLC with high concordance between cytology and histology of 97% and 93% respectively. Despite the lower sensitivity for non keratinizing SQC the specificity of this diagnosis is very high which measures that the false positivity of SQC is extremely rare. Thus having proved overall high accuracy of cytology in distinguishing SQC versus non SQC, it was concluded that cytology speciality is suitable for guiding therapeutic decisions within these diagnostic categories. There is increasing awareness that the quality of specimens such as cytology has a profound influence on molecular diagnostic test results than the resected tissue specimens.

Conclusion

The field of thoracic oncology is going through a revolution with the advent of targeted therapy for the management of patients with lung cancer. FNAC is in many cases the only diagnostic specialty available for guiding therapeutic decisions. FNAB has proven to be an invaluable tool not only for diagnostic accuracy of pulmonary carcinoma but also a reliable and adequate source of material suitable for molecular analysis.

Ethical Clearance

Obtained from ethical committee.

Source of Funding

Self

Conflict of Interest

NIL

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