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Fine needle aspiration cytology and correlation with biopsy in lung lesions

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Abstract
Introduction: Lung cancer is one of the leading cause of death worldwide. High mortality makes early diagnosis and treatment of utmost importance. Cytology plays an important role in the initial evaluation and diagnosis of these patients. Currently various sampling techniques are available to procure specimens for cytologic evaluation, which include exfoliative, abrasive cytology and fine needle aspiration cytology (FNAC). The aim of the study is to assess the role of CT/USG guided FNAC of lung and pleural lesions and correlate the findings with biopsy
Methods: 82 patients with lung lesions were evaluated with USG/CT guided FNA and biopsy between January 2016 & July 2016. The findings of FNAC were correlated with the biopsy wherever available, in order to assess the reliability of a cytologic diagnosis of the various lung lesions on FNAC. The various differential diagnosis are also discussed.
Results: The age group ranged from 19-84ys with a median age of 60 yrs, and a male predominance (92.6%). Majority of lesions involved the lung parenchyma. Benign, suspicious and malignant lesions accounted for 8.5%, 3.7% and 87.8% respectively. On classification, adenocarcinomas accounted for majority of the malignant lesions (34.1%) followed by squamous cell carcinomas (26.8%). 57 out of 82 patients underwent biopsy of the lung lesions. When the FNAC findings were correlated with the histopathological biopsy findings, 6.7 % (4) of cases did not correlate. Thus the sensitivity and specificity of the study were 84.2% and 100% respectively. Preoperative diagnosis of lung cancer detected by screening with CT could be reliably made by FNAC. Difficulty in classification occurs in carcinomas of high nuclear grade with prominent nucleoli, including poorly differentiated squamous cell carcinoma and large cell neuroendocrine carcinoma. Differentiating adenocarcinoma and squamous cell carcinomas could also be challenging at times.
Conclusion: CT guided FNAC has emerged as a less invasive, cost effective, rapid and fairly accurate diagnostic aid in the evaluation of lung lesions. Correlation of the cytomorphologic features with the clinical presentation of the patient including radiologic imaging are absolutely critical in the accurate interpretations of respiratory cytology specimens.

Keywords: lung, cytology, FNAC

Introduction

Lung cancer is by far the leading cause of cancer death among both men and women. With the advent of targeted therapy for the management of patients with lung cancer, the field of thoracic oncology is going through a revolution [1, 2]. Majority of patients with lung cancer are treated with systemic therapies since they present with clinically advanced disease, hence not being fit for surgical resection [2, 3, 4]. Cytology plays an important role in the initial evaluation and diagnosis of these patients. Various sampling techniques available include exfoliative and abrasive cytology, fine needle aspiration cytology (FNAC) and cell block preparations [3, 4, 5, 6]. Ultrasound guided (USG) / Computerized tomography(CT) guided fine needle aspiration biopsy (FNAB) play a very important role in initial diagnosis [7, 8, 9].
FNAB in many cases proves to be the only diagnostic specimen available for definitive diagnosis, sub classification, including molecular studies and guiding therapeutic decisions in lung cancer. Thus proving to be a valuable diagnostic tool. The aim of the present study was to assess the role of USG/ CT guided FNAC of lung lesions and correlate the findings with biopsy.

Materials and methods

A retrospective study was conducted on 82 patients with lung lesions which were evaluated with USG/CT guided FNAC and biopsy, for a period of 6 months. The cytology smears were stained with Papanicolaou stain and the biopsy examined using hematoxylin and eosin stain. The findings and diagnosis of FNAC were correlated with the biopsy wherever available, in order to assess the reliability of a cytologic diagnosis of the various lung lesions on FNAC. The lung lesions were classified into non neoplastic and neoplastic lesions. The neoplastic lesions were further classified and compared with the biopsy findings where ever available. SPSS v25 software was used for statistical analysis.

Results

On analysis, the age group of the patients ranged between 19-84ys with a median age of 60 yrs. A male predominance (92.6%) was noted. Majority of lesions involved the left lung parenchyma (75.7%). Breathlessness (63.4%), fever (58.5%) followed by cough (46.3%) were the main presenting symptoms. Others included chest pain, weight loss and hemoptysis. [Table 1]

The lesions were categorized as non-neoplastic (Inflammatory/Benign), suspicious for neoplasia and malignant lesions, which accounted for 8.5%, 6.1% and 85.4%espectively. The malignant lesions were further subtyped. [Table 2]

On classification of the malignant lesions, adenocarcinomas accounted for majority of the malignant lesions (34.1%) followed by squamous cell carcinomas (26.8%).[Table 3] The other category of lesions were large cell neuroendocrine carcinoma, small cell carcinoma, poorly differentiated carcinoma, adenosquamous carcinoma, non Hodgkins lymphoma and metastatic carcinoma.

Only 57 out of 82 patients underwent biopsy of the lung lesions. When the FNAC findings in these cases were correlated with the histopathological biopsy findings, 6.7 % (4) of cases did not correlate. [Table 4]. Thus the sensitivity and specificity of the study were 84.2% and 100% respectively.

The four cases which did not correlate with biopsy were in the malignant category. All four cases were reported to be malignant. However on subtyping on biopsy, three cases which were thought to be poorly differentiated carcinomas on FNAC turned out to be poorly differentiated squamous cell carcinomas. One case which was reported as adenocarcinoma on FNAC showed adenosquamous features on biopsy.

Discussion

Introduced by Leyden in 1883 and Menbriel in 1986, the diagnostic lung puncture technique has long been used for the identification of infections and malignancy with high accuracy [1, 9, 10]. Following various advances in radiology, USG /CT guided FNAC of lung lesions is very helpful to arrive at a definitive diagnosis in infectious and neoplastic lesions though it is of utmost importance in diagnosis of malignancy [2, 5, 6, 11]. It is also a safe and accurate method with pneumothorax being reported in a few studies as a post procedure complication. FNAC can be even combined with Rapid on-site evaluation (ROSE) as described by Fassina *et al*. [6] It has been found that ROSE is also a safe and useful tool in the diagnostic work-up of lung cancer patients.

In the present study, a male preponderance is observed which is in concordance with other studies. Patients present with a wide variety of symptoms which include cough, fever, shortness of breath, chest pain, loss of weight and haemoptysis. Rarely hoarseness of voice may also be observed [3, 4, 9]. In the present study in most common clinical symptom observed was breathlessness followed by fever and cough.

In the non-neoplastic category, three cases showed non-specific inflammatory cells. Three other cases showed granulomas with chronic inflammation with only one case showing AFB positivity. Another case showed slender branching septate hyphae suggestive of aspergillus. With respect to granulomatous lesions, 12 cases have been reported by Gangopadhyay M *et al.*, 9 cases by Sengupta M *et al.* and 15 cases by Ahmed Z *et al.* [2, 3, 4, 5]. One case each of aspegillus infection has been reported by Gangopadhyay M *et al.* and Sengupta M *et al.* Two cases of histoplasmosis have been reported by Sengupta M *et al.* [Table 5]

In the neoplastic category, about 70% of the primary lung cancers are diagnosed as non-small cell carcinomas, whereas small cell carcinomas account for about 20%. In the present study, a similar pattern was observed with adenocarcinomas accounting for the most common type accounting for 34.1%. Studies of Madan m & bannur h, Gangopadhyay M *et al.*, Mondal SK *et al.* and Sengupta M *et al.* also show a similar pattern [1, 2, 3, 4,] [Table 5]. However Ahmed Z *et al.* have reported a predominance of squamous cell carcinomas in their study accounting for 35% compared to adenocarcinoma accounting for 25 % in their study. Various other category of malignant lesions were also found [Table 5]

Difficulty in classification occurs in carcinomas of high nuclear grade with prominent nucleoli, including poorly differentiated Squamous cell carcinoma and large cell neuroendocrine carcinoma. Differentiating adenocarcinoma and squamous cell carcinomas could also be challenging at times. Table 6 gives a detailed description of the cytomorphology in different lung malignancies.

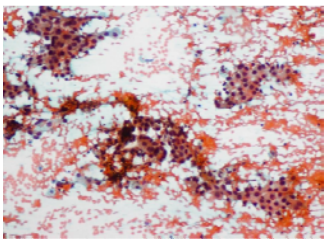

Fig 1: Adenocarcinoma with cells arranged in cluster and acinar pattern. [Pap x100]

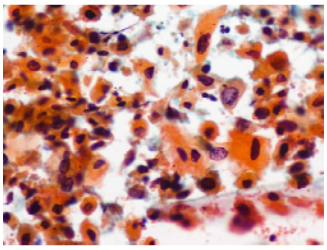

Fig 2: Squamous cell carcinoma with sheets of dysplastic and keratinized cells [Pap x200]

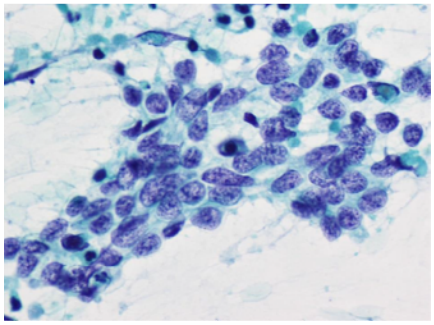

Fig 3: Large cell neuroendocrine carcinoma with clusters of cells showing large nuclei with granular chromatin [Pap x200]

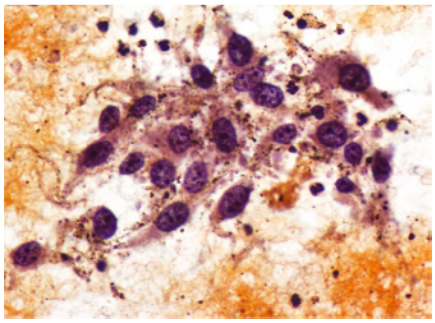

Fig 4: Metastatic malignant melanoma with cells having vesicular nuclei and melanin pigment [Pap x200]

Table 1: Clinical details of patients

Clinical details	Number	Percentage
Sex		
Male	76	92.6%
Female	6	7.4%
Laterality		
Right	20	24.3%
Left	62	75.7%
Smoking History	60	73.1%
Clinical features		
Fever	48	58.5%
Breathlessness	52	63.4%
Cough	38	46.3%
Chest pain	27	32.9%
Weight loss	30	36.5%
Hemoptysis	18	21.9%

Table 2: Categories based on FNAC

Cytological diagnosis	Number	Percentage
Non neoplastic (Inflammatory / Benign)	7	8.5%
Suspicious for malignancy	5	6.1%
Malignant	70	85.4%
Total	82	100

Table 3: Various categories of lung lesions

Cytological diagnosis	Number	percentage
Non neoplastic(Inflammatory / Benign)		
Inflammatory	3	3.6
Granulomatous	3	3.6
Aspergillosis	1	1.2
Suspicious for malignancy	5	6.1
Malignant lesions		
Adenocarcinoma	28	34.1
Squamous cell carcinoma	22	26.8
Large cell neuroendocrine carcinoma	1	1.2
Small cell carcinoma	6	7.3
Poorly differentiated carcinoma	9	11.0
Adenosquamous carcinoma	1	1.2
Non Hodgkins lymphoma	1	1.2
Metastatic carcinoma	1	1.2
Metastatic malignant melanoma	1	1.2
Total	82	100

Table 4: Correlation of FNAC and Biopsy

FNAC and Biopsy correlation	Number	Percentage
Correlated	53	92.9
Not correlated	04	7.1
Total	57	100

Table 5: Comparison of the present study with various other studies with respect to the category of lung lesions

Category of lesions	Subcategory of lesions	Present study	Madan m & bannur h (lung 4)	Gangopadhyay M *et al.*	Mondal SK *et al.*	Sengupta M *et al.*	Ahmed Z *et al.*
Inflammatory / Benign	Inflammatory lesions	3	12	14	10	12	17
	Granulomatous lesions	3	1	12		9	15
	Histoplasmosis	0	0	0		2	0
	Aspergillus	1	0	1		1	0
Suspicious for malignancy	Suspicious for malignancy	5	1	2	0	6	0
Malignancy	Adenocarcinoma	28	12	52	60	8	25
	Squamous cell carcinoma	22	9	24	26	5	35
	Large cell neuroendocrine carcinoma	1	0	1	0	0	0
	Small cell carcinoma	6	0	8	17	6	6
	Poorly / undifferentiated carcinoma /Non-small cell NOS	10	3	2	0	10	2
	Adenosquamous carcinoma	1	0	0	0	0	0
	Non Hodgkins lymphoma	1	0	3	0	2	0
	Hodgkins lymphoma	0	0	1	0	0	0
	Plasmacytoma	0	0	1	0	0	0
	Fibrosarcoma	0	0	1	0	0	0
	Germ cell tumor/Seminoma	0	0	1	0	1	0
	Melanocarcinoma	0	0	1	0	0	0
	Carcinoid	0	0	0	6	0	0
	Broncho-alveolar carcinoma	0	0	1	2	1	0
	Spindle cell neoplasm	0	0	0	1	1	0
	Large cell anaplastic carcinoma	0	0	0	2	0	0
	Malignant melanoma	1	0	0	0	1	0
	Metastatic carcinoma	1	0	0	0	2	0
Inadequate	Inadequate	0	2	2	0	6	0
	Total	82	40	127	124	74	100

Table 5: Cytological features of malignant lesions in lung

Malignancy	Cytological features
Squamous cell carcinoma	Sheets and clusters of cells with enlarged, dense, hyperchromatic, angulated nucleus with irregular distribution of chromatin, inconspicious nucleoli, orangeophilic cytoplasm
Adeno-carcinoma	Acinar pattern, cells with abundant cytoplasm, round to oval nucleus, conspicious nucleoli, intracytoplasmic mucin +/- Glandular and papillary forms may be sometimes present
Small cell carcinoma	Clusters and rosettes of cells with scant cytoplasm, nuclear moulding, salt & pepper chromatin
Large cell neuroendocrine carcinoma	Highly pleomorphic large cells arranged in sheets and clusters.

Conclusion

Preoperative diagnosis of lung cancer detected by screening with CT could be reliably made by FNAC. Correlation of the cytomorphologic features with the clinical presentation of the patient including radiologic imaging are absolutely critical in the accurate interpretations of respiratory cytology specimens.

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