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Cell blocks histopathology versus FNA cytology in diagnosis of primary malignant lung mass: A comparative study

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Abstract

Background and objective: Fine needle aspiration cytology with cell block preparation is widely used for preoperative confirmation of solitary lung mass and classification of the histologic types. This study aimed to highlight the importance of cell-block preparation in the diagnosis of primary malignant lung lesion by comparing cytomorphological preservation on paired cell block and conventional fine needle aspiration samples.

Methods: During January 2012 to October 2015, a total of 100 cases with solitary lung mass were included, either visited Rizgary Teaching Hospital or Walfare private hospital. All the patients had undergone fine needle aspiration and cell block preparation under a CT-guide.

Results: The samples were evaluated by the fine needle aspirations and cell blocks preparations from primary lung lesion under a CT-guide. 74% were male, and the majority of them were in the sixth and seventh decade. Squamous cell carcinoma was the most common histologic type consisting 42% of the studied cases, followed by adenocarconima (31%), small cell carcinoma (19%) and the remaining 8% were large cell carcinomas. In the assessment of agreement of cellularity between the two methods of sample preparation, cell block served better than fine needle aspiration (P = 0.715). However, this difference was statistically non-significant. A significant relation was found for morphology which was preserved in fine needle aspiration samples better than that in cell block samples (P <0.05). In contrast, all cell block samples displayed a statistically highly significant architectural preservation compared to fine needle aspiration samples (P <0.001). The sensitivity and specificity of the present study were 98.46%, 99.2% respectively.

Conclusion: Direct fine needle aspiration smears and cell blocks complement each other, and our results indicate that both are needed in the diagnostic work-up of patients with a primary malignant lung mass.

Keywords: Cell block; Fine needle aspiration; Lung mass.

Introduction

Primary lung cancer is, without a doubt, the number one cause of cancer-related deaths in many countries. Unfortunately, the most common cause of mass in the lungs is lung carcinomas. Other causes of lung mass include other cancers that may appear as a mass in the lungs are lymphomas and sarcomas. Benign lung tumors include hamartomas, metastases, lung abscesses, arteriovenous malformations, infections, pulmonary artery aneurysms, and amyloidosis.[1] Among the four major histologic subtypes of primary lung cancers, squamous cell carcinoma, adenocarcinoma, small cell carcinoma, and large cell carcinomas, small cell carcinoma is distinct. Small cell carcinomas are best treated by chemotherapy because they are metastatic at presentation; while the others are usually curable by surgery.[1] Fine needle aspiration (FNA) of tumors is an approach that is widely used for diagnosis of solitary lung lesion. It involves aspiration of cells from a mass followed by the cytologic examination of the prepared

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smear. Although this procedure is used most commonly with readily palpable lesions, modern imaging techniques such as computed tomography (CT) scan allow extension of the method to deeper structures such as lung and liver, which obviates surgery and its attendant risks.[2] Fine needle aspiration cytology (FNAC) not only distinguishes between benign and malignant lesions but also helps in tumor typing of lung cancer, so specific therapy such as chemotherapy or surgery, if possible, can be initiated without unnecessary delay. Apart from some difficulties, such as small sample size, it can be extremely reliable, rapid and useful in experienced hands. Therefore, FNAC is a simple, relatively safe technique for the diagnosis of pulmonary mass lesions, particularly with the aid of (CT) scan,[3] but one of its limitations is the limited amount of materials available for adjuvant diagnostic investigations. They found that with the use of the cell block technique, we can retrieve small tissue fragments in a fluid specimen which are processed to form tissue paraffin block. It has been widely accepted that this method of analysis will not only increase the cellular yield but also improves diagnostic accuracy.[4,5] This study aimed to highlight the importance of cell-block method in the diagnosis

Methods

of primary malignant lung lesions by comparing cytomorphological preservation on paired cell block and conventional fine needle aspiration samples. This retrospective study was performed in the Radiology Departments at Rizgary Teaching Hospital and Welfare private hospital. Hundred FNAs were carried out by trained personnel from January 2012 to October 2015. Material from lung lesions was aspirated for conventional smears and cell block preparation simultaneously. The samples were obtained following local anesthesia using a standard 21 gauge needle attached to a 20 ml syringe. After localization, the needle was passed gently through the lesion five to ten times with aspiration. The needle was withdrawn, direct smears were prepared from part of the sample, and the remaining samples were preserved in 10% neutral buffered formalin, processed routinely, and stained with haematoxylin and eosin for cell block sections. The specimens were examined and reported by cytopathologist and histopathologist. A comparison between the grading of cellularity, morphological and architectural preservation was performed on paired FNA smears and cell block samples according to the grading system,[6] as shown in Table1.

Statistical Analysis Used:

Statistical analysis was done by using the statistical package for the social sciences (version 19) computer software. A *P* value of ≤0.05 was regarded as statistically significant and <0.001 as highly significant. Cross tables and associations between different variables were measured using Chi-square test. Fisher exact, Wilcoxon-rank sum and McNemar tests were used when needed.

Table 1: The grading system.

Score	Description
Cellularity	
0	No cells
1+	Low (tumor cells represent <10% of cells present)
2+	Moderate(tumor cells represent 10-50% of cells present)
3+	High(tumor cells represent >50% of cells present)
Morphological preservation	Presence or absence of clear nuclear membrane,
0	Poorly preserved
1+	Well preserved
Architectural preservation	Presence or absence of clear tissue architectural arrangement
0	Absent
1+	Present

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Results

A total of 100 cases were included in the study with adequate FNAC smear and cell block report of primary lung masses. Seventy-four cases (74%) were male and 26 (26%) were female. The age ranged from 45 years to 78 years. There were thirteen cases below 50 years of age, and the remaining 87 cases were older than 50 years. Squamous cell carcinoma was the commonest lesion, (42%), followed by adenocarconima (31%). There were 19 cases (19%) of small cell carcinoma and the remaining 8 cases (8%) with large pleomorphic, undifferentiated cells were grouped as large cell carcinomas (Table 2). The cases of squamous cell carcinoma showed sheets and clusters of pleomorphic squamous cells with abundant cytoplasm and hyperchromatic nuclei. Few cases showed keratinization. The cases of adenocarcinoma, on the other hand, showed tumor cells arranged in a glandular pattern and the cells had round nuclei with prominent solitary nucleoli. The highly cellular smears with smaller cells having scanty cytoplasm, salt and pepper chromatin and nuclear molding were grouped as small cell carcinomas (Figures 1, 2 and 3).

Table 2: Distribution of sample by histologic types.

Histologic type	No. (%)
Squamous cell carcinoma	42 (42%)
Adenocarconima	31 (31%)
Small cell carcinoma	19 (19%)
Large cell carcinomas	8 (8%)
Total	100 (100%)

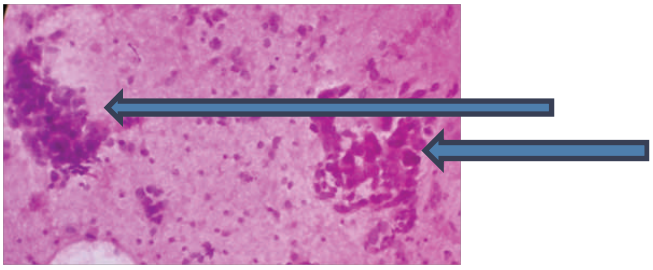

Figure 1: Cytological smear, lung mass (H&E stain×400).

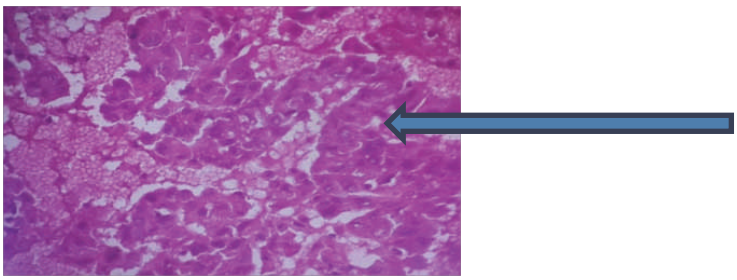

Figure 2: Cell block section, lung mass (H&E stain×400).

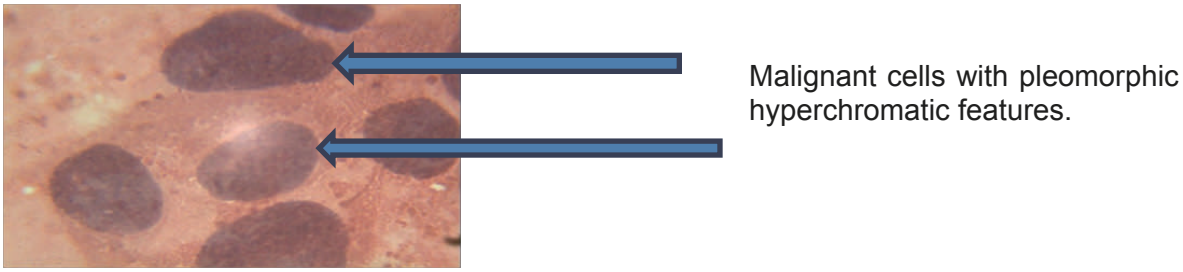

Figure 3: FNA, lung mass (H&E stain×1000).

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There was no statistically significant association between age and histological types. Gender was significantly associated with the histological types (P <0.001). Out of 74 male patients, 33 (44.6%) presented with squamous cell carcinoma type, 15 (20.27%) with adenocarcinoma, 19 (25.68%) with small cell carcinoma and the other 7 (9.46%) with large cell carcinomas. In females, 9 (36.61%) patients presented with squamous cell carcinoma, 16 (61.54%) with adenocarcinoma, no female patient presented with small cell carcinoma and only one patient (3.85%) presented with large cell carcinoma0.001 (Table 3). In 17 cases we used Immunohisto-chemistry (IHC) i.e. carcinoembryonic antigen (CEA), high molecular weight keratin (HMW keratin) and Chromogranin for confirmation of the diagnosis of histological type. In the assessment of agreement of cellularity between the two methods in sample preparation, cell block serves better than FNA as 55 cases showed high tumor cells (+3) compared with 35 cases by FNA procedure, *P* = 0.715, as shown in Table 4.

Table 3: Relation between sex, age and histological types.

Clinical variables		Histologic types				*P* value
		Squamous cell carcinoma	Adenocarcinoma	Small cell carcinoma	Large cell carcinoma	
		Number (%)	Number (%)	Number (%)	Number (%)	
Gender	Female	9 (34.61%)	16 (61.54%)	0 (0%)	1 (3.85%)	<0.001*
	Male	33 (44.6%)	15 (20.27%)	19 (25.68%)	7 (9.46%)	
Age	<50	7 (53.85%)	4 (30.77%)	2 (15.38%)	0 (0%)	0.798*
	>50	35 (40.23%)	27 (31.03%)	17 (19.54%)	8 (9.2%)	

*Fisher exact test used.

Table 4: Cell block versus FNA in grading cellularity.

Score		FNA Number (%)	Cell block Number (%)	*P* value
Cellularity	0	5 (5%)	2 (2%)	0.715*
	+1	10 (10%)	8 (8%)	
	+2	50 (50%)	35 (35%)	
	+3	35 (35%)	55 (55%)	
	+1	72 (72%)	100 (100%)	

*Wilcoxon signed –rank sum test used.

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In FNA samples morphology was preserved in 95 (95/100) samples compared to 87 samples (87/100) in cell block samples, *P* <0.05, as shown in Table 5. All cell block samples (100/100) displayed architectural preservation compared to only 72 FNA samples (72/100), *P* <0.001, as shown in Table 6. The sensitivity and specificity of the present study were 98.46% and 99.2%, respectively.

Discussion

The use of cell blocks has been widely advocated in the diagnostic work-up of patients with masses amenable to FNA since they provide diagnostic architectural information which complements FNA smears.[7] CT guided FNAC of pulmonary masses provides a simple, easy, and reliable method for reaching rapid tissue diagnosis with minimal complication.[8] In the current study, most of the cases were male (74%), that's in agreement with the result of Saha et al.,[8] Mondal et al[3] and others.[9,10] Age distribution of our cases was mostly in the sixth and seventh decade. This is in agreement with studies done by Monda et al. and Saha et al.[3,8] Squamous cell carcinoma was the most common malignant lesion, which was followed by adenoarcinoma and then 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.[9] and Madan et al.,[11] where as in certain other studies, prevalence of squamous cell carcinoma was more than adenocarcinoma.[10,12-14] In the present study, the relation between male gender and histologic type of diseases is highly significant, which may be due to the high percentage of smackers among male in our population that proved to have an important relation to squamous cell carcinoma type. This is in agreement with a study done by Mondal.[3] In this study, FNA smear was the better method for routine diagnosis due to the superior preservation of nuclear and cytoplasmic characteristics while the cell block technique serves better for presence or absence of clear tissue architectural arrangement, especially in adenocarcinoma.

Table 5: Cell block versus FNA in grading morphological preservation.

		Cell block		Total	*P* value
		0 No. (%)	+1 No. (%)		
FNA	0	5(5%)	0(0%)	5(5%)	**0.008
	+1	8(8%)	87(87%)	95(95%)	
Total		13(13%)	87(87%)	100(100%)	

**McNemar test used.

Table 6: Cell block versus FNA in grading architectural preservation.

		Cell block		Total	*P* value
		0 No. (%)	+1 No. (%)		
FNA	0	0(0%)	28(28%)	28(28%)	**<0.001
	+1	0(0%)	72(72%)	72(72%)	
Total		0(0%)	100(100%)	100(100%)	

**McNemar test used.

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There was a poor agreement and statistically significant difference between methods in the assessment of morphological preservation (P <0.05) and architectural preservation (P <0.001). Like our results, Khan found that there was no overall agreement in the preservation of cytomorphological detail between the two methods, and the conventional FNA smears served better than the cell block for the evaluation of nuclear and morphologic characteristics.[15] Similarly, Thapar reached to result that using a combination of the cell block and smear techniques yielded 13% more malignant cases than what were detected using smears by themselves.[16] The variation in technique may have contributed to either the success or failure of obtaining adequate samples which are largely dependent on the skill of the aspirator and high cellularity of the aspirate. The sensitivity and specificity of the present study are comparable to that of Khouri et al.,[17] Hamper et al.[18] and Rangaswamy et al.[19] In a study done by Mondal, CT guided FNAC showed almost perfect agreement with histological diagnosis.[3] So FNAC was found to be highly accurate (95%) in the diagnosis of lung mass as almost similar finding was shown by previous studies.[11,20] 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. Numerous studies supported that CT-guided FNAC with cell block preparation is an accurate and sensitive way of diagnosing malignancy of the lung.[21] This procedure is almost minimum painful non-operative procedure as compared with biopsy for diagnosis of pulmonary mass, outweighs the only major rare complication of pneumothorax. FNAC has long been used for the non-surgical confirmation of primary as well as metastatic thoracic lesions. The particular advantage of FNAC includes detection of those tumor types like small cell carcinoma, more appropriately treated with chemotherapy rather than surgery,[3] cell block study was instrumental in offering a conclusive opinion in cases where the cytologic findings were inconclusive, cell block sections helped us in reaching a more conclusive diagnosis. The cell block technique not only increased the positive results but also helped to demonstrate better architectural patterns, which could be of great help in making the correct diagnosis of the histological type.

Conclusion

Cell blocks complement FNA smears in preoperative diagnosis of primary malignant lung mass and subclassify histological types. Future research in this field would benefit from exploring preparing cell block samples and, FNA smears for immunohistochemistry (IHC) study, another recommendation is bronchoscopic/ trucut biopsy/lobectomy evaluation simultaneously with cytological smears and cell block to reach a definite diagnosis.

Conflicts of interest

The authors report no conflicts of interest.

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