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Pathology

CYTOHISTOMORPHOLOGICAL SPECTRUM OF LUNG LESIONS AT A TERTIARY CARE CENTRE: CROSS SECTIONAL STUDY

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ABSTRACT **INTRODUCTION** Despite advances in diagnostic techniques, lung lesions remain a significant diagnostic challenge, and there is a need to investigate the cyto-histomorphological spectrum of lung lesions in order to improve the diagnostic accuracy and patient outcomes. **AIM** To evaluate the cyto-histomorphological spectrum of lung lesions. **MATERIALS AND METHODS** A cross-sectional study was done on 140 adequate lung samples [bronchoalveolar lavage (BAL), radiologically guided fine needle aspiration (FNA), bronchoscopic biopsy and CT-guided biopsy] received in the Department of Pathology from 113 patients. The cyto- and histo-logical examinations were done. **RESULTS** Maximum pulmonary pathologies were seen in the males of seventh decade involving right side of the lung more than the left side. The commonest finding in BAL was inflammation (47.5%), in radiologically guided FNA was adenocarcinoma (46.6%) and in biopsy was squamous cell carcinoma (25.7%). BAL was 18.75% sensitive, 100% specific and 51.85% accurate compared to histology. Immunohistochemistry (IHC) and special stain aided in accurate diagnosis of 11 cases which were equivocal on histology. **CONCLUSION** It is crucial to know the spectrum of lung lesions for accurate diagnosis. For diagnosing a lung lesion, it is reasonable to use BAL in suspected cases due to its high specificity because if BAL tests positive, it is highly likely that the disease is present. The combined use of cytology and histology gives better results. If further required, IHC will also help in proper subtyping of the malignant lesion.

KEYWORDS : BAL; Biopsy; Cyto-histological correlation; Cyto-histomorphological spectrum; Guided FNA; IHC; Lung lesions

INTRODUCTION

Respiratory diseases have become very common these days. The cases where a definitive diagnosis could not be established by clinical, radiological and routine laboratory evaluation, the pathological examination of the cells or biopsy tissue becomes necessary to reach to a definitive diagnosis.[1] For the management of chest diseases, fiber optic bronchoscopy has been adorned as an essential diagnostic and therapeutic tool. It has revolutionized the practice of pulmonary medicine.[2,3] Diagnostic cytology is an appropriate modality for non-neoplastic as well as neoplastic diseases of lung.[4] The cases in which high-resolution CT and BAL could not establish the diagnosis, bronchoscopic lung biopsy should be considered. In numerous conditions, bronchoscopic lung biopsy can form the diagnosis and surpass the requirement of surgical lung biopsy.[5] It is an important and technically easy-to-use tool for diagnosing endobronchial neoplasms along with inflammatory conditions.[6-12] IHC is required for confirmation in few cases where diagnosis could not be confirmed by histopathological findings.[13] Its use for diagnosing surgical pathology has changed the practice of pathology, as its use is more widespread with more available antibodies to enhance diagnostic specificity.[14]

MATERIALS AND METHOD

INCLUSION CRITERIA:

i. Adequate specimens.
ii. All the BAL, radiologically guided FNA specimens along with bronchoscopic and CT guided biopsy specimens of lung lesions.
iii. Clinical details to be available for correlation.

EXCLUSION CRITERIA:

i. Inadequate specimen.
ii. Specimens which are autolysed and have disrupted cellular morphological details or technical shortfalls.
iii. Inadequate clinical details.

The specimens of BAL for cytological examination and biopsy for histologic confirmation of the diagnosis were obtained through flexible fibreoptic bronchoscope by the pulmonologist. The specimens of radiologically guided FNA and CT guided biopsy for analysis were obtained by pathologist with the help of radiologist. These specimens were obtained in The Department of Pathology, S. N. Medical College, Agra along with the relevant clinical details of the patient. These were further processed for analysis. The equivocal cases of lung masses on histology were put through IHC by routine antigen retrieval method for verification and typing of lesions.

RESULTS

Lung lesion samples were received from a total of 130 patients, out of which 17 were inadequate. Hence, 113 cases were analyzed for this study. The cases had a wide age range, i.e., from 2nd to 9th decade of life. However, maximum patients were seen in the 7th decade (38.9%) followed by 6th decade (24.7%). The mean age was 59.15 years. 86 (76.1%) cases were males and 27 (23.9%) were females. The male to female ratio came out to be 3.18:1. The commonest primary site of lesion was right lung (54.8%).

Among 113 cases, there were 27 such cases where both cytological and histological specimens were available, 47 cases had only cytological specimens and 39 cases had only histological specimens. Hence, there were 74 cytological specimens and 66 histological specimens for examination comprising 140 specimens in total.

Out of 74 cytological specimens (BAL and radiologically guided FNA), maximum cases (39.2%) showed inflammation and 24.3% cases were reported as malignant. Among the malignant cases, adenocarcinoma was the commonest.

Table-1: Allocation of cases according to cytological examination

Cytological diagnosis	Number of cases	Percentage
Normal	23	31%
Inflammation	29	39.2%
Fungal lesion	1	1.4%
Atypical	1	1.4%
Suspicious for malignancy	2	2.7%
Malignant	18	24.3%

Total	74	100%

Table-2: Allocation of malignant cases diagnosed on cytology

Malignancy	Number of cases	Percentage
Adenocarcinoma	7	38.9%
Squamous cell carcinoma	5	27.8%
Non-small cell carcinoma, favor adenocarcinoma	3	16.6%
Poorly differentiated carcinoma	2	11.1%
Metastasis	1	5.6%
Total	18	100%

Out of 66 histological specimens, maximum cases (50%) were malignant and squamous cell carcinoma was the commonest malignant lesion.

Table-3 Allocation of cases based on histological examination

Diagnosis on histology	Number of cases	Percentage
Normal	8	12.1%
Inflammation	12	18.1%
Necrosis	1	1.6%
Fungal lesion	3	4.5%
Solitary fibrous tumor	1	1.6%
Suspicious for malignancy	8	12.1%
Malignant	33	50%
Total	66	100%

Table-4: Allocation of malignant cases diagnosed on histology

Malignancy	Number of cases	Percentage
Squamous cell carcinoma	17	51.5%
Adenocarcinoma	9	27.3%
Poorly differentiated carcinoma	3	9.1%
Non-small cell carcinoma with adenocarcinoma and squamous differentiation	2	6.1%
Small cell carcinoma	1	3%
Mesenchymal lesion	1	3%
Total	33	100%

Out of 66 biopsy specimens, there were 12 cases which were equivocal on histopathology, i.e., a concrete diagnosis could not be established on histological examination. So, they were further analysed with IHC. Out of these, one case of poorly differentiated carcinoma could not be further analysed as the paraffin wax block was not available. Hence, it was diagnosed as Non-Small cell carcinoma, NOS. Rest of the 11 cases were analysed with IHC.

Table-5 : Diagnosis established after IHC and special staining

Histological diagnosis	Number of cases	Stain used	Diagnosis
Suspicious for malignancy	4	p40 positive	Squamous cell carcinoma
Suspicious for malignancy	2	TTF1 positive	Adenocarcinoma
		p40 negative	
Suspicious for malignancy	2	AE1/AE3 positive	†SmCC
*PDCA	1	TTF1 positive	Non-†SmCC, favor
		p40 negative	
*PDCA	1	TTF1 negative	Non-small cell carcinoma, favor adenocarcinoma
		p40 negative	
		PAS positive	
Mesenchymal lesion	1	Vimentin positive	Metastasis
		CD68 positive	

†SmCC – Small cell carcinoma
*PDCA – Poorly differentiated carcinoma

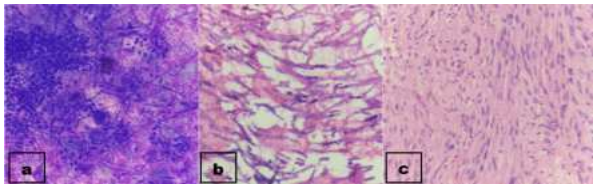

Figure-1: a) BAL - Fungal spores and hyphae (MGG, 1000x). b) Bronchial biopsy- Aspergillus (H&E, 400x). c) CT-guided biopsy - Solitary fibrous tumour (H&E, 400x)

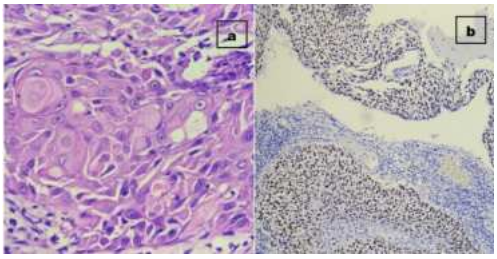

Figure-2: a) Bronchial biopsy – Squamous cell carcinoma (H&E, 400x). b) p40 positive - Squamous cell carcinoma (IHC, 100x).

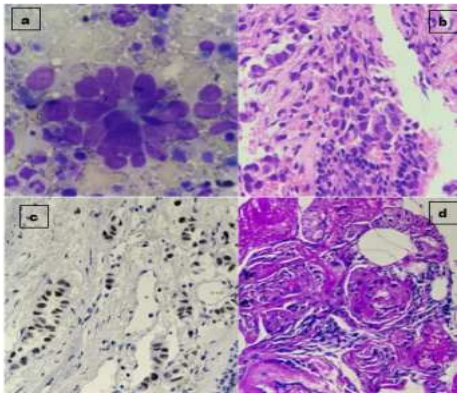

Figure-3: a) Guided FNA- Adenocarcinoma (MGG, 1000x). b) Bronchial biopsy- Adenocarcinoma (H&E, 400x). c) TTF1 positive - Adenocarcinoma (IHC, 400x). d) PAS positive - Non small cell carcinoma, favour adenocarcinoma (Special stain, 400x).

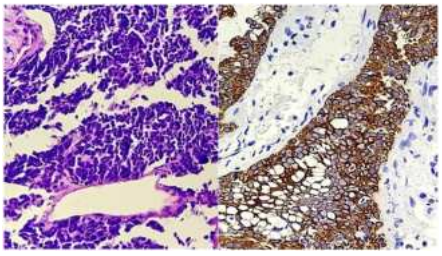

Figure-4: a) Bronchial biopsy – Small cell carcinoma (H&E, 400x). b) AE1/AE3 positive - Small cell carcinoma (IHC, 400x).

Out of 27 cases of BAL with simultaneous biopsy specimens, 40.7% cases were concordant. For these 27 cases, the malignant and suspicious for malignancy cases were categorized under neoplastic lesions and rest of the cases were categorized under non-neoplastic lesions.

Table-6: Statistical values of BAL with respect to histopathological examination

Sensitivity	Specificity	*PPV	†NPV	Diagnostic accuracy
18.75%	100%	100%	45.83%	51.85%

*PPV – Positive predictive value
†NPV – Negative predictive value

DISCUSSION

Usually, cytology gives a result which comes out to be comparable with biopsy. But sometimes, it becomes very difficult to diagnose the case on cytology alone. For this, biopsy is required for histopathological examination and if in few cases, even histopathology could not confirm the diagnosis, IHC rescues the pathologist to make an accurate diagnosis.[13]

In this study, BAL showed non-neoplastic cases (89.8%) more than the neoplastic cases (10.2%). Other studies like Kedige AR et al[1], Pavani M et al[15], Tyagi G et al[16], Tiwari A et al[17], Sharma S et al[18], Chothani K et al[19], Gundewar M et al[4], Ghildiyal S et al[20] and Sareen R et al[21] also showed similar finding of non-neoplastic cases more than the neoplastic cases. On the other hand, in few studies like Joshi J et al[22]

and Dhanalakshmi S et al[23], BAL showed neoplastic cases more than the non-neoplastic cases.

The most common neoplastic diagnosis in BAL in this study was squamous cell carcinoma (5.1%). Similar observation regarding the most common neoplastic finding on BAL was done by Kedige AR et al[1], Sharma S et al[18], Gundewar M et al[4], Dhanalakshmi S et al[23], Sareen R et al[21] and Bhat N et al[24]. Two studies, namely Pavani M et al[15] and Tomar V et al[25] were discordant with this observation as the most common neoplastic finding on BAL in their study was adenocarcinoma.

The radiologically guided FNA in our study showed that the neoplastic findings (93.3%) were more than the non-neoplastic findings (6.7%). This was similar to the studies of Dhar O et al[13], Tomar V et al[25] and Sareen R et al[21].

The most common neoplastic diagnosis in radiologically guided FNA in our study was adenocarcinoma (46.6%). This was in compliance with studies conducted by Dhar O et al[13] and Tomar V et al[25]. On the other hand, Sareen R et al[21] observed squamous cell carcinoma as the most common neoplastic diagnosis in radiologically guided FNA.

This study was similar to various studies like Kedige AR et al[1], Goel S et al[26], Tiwari A et al[17], Joshi J et al[22], Sireesha VJB et al[27], Dhanalakshmi S et al[23], Tomar V et al[25] and Bhat N et al[24], where the histological diagnosis showed that the neoplastic cases diagnosed were more than the non-neoplastic cases. Few studies like Tyagi G et al[16] and Gundewar M et al[4] showed discordance with this study as in their study, non-neoplastic cases were found more than the neoplastic cases in histology.

The commonest histological neoplastic finding in this study was squamous cell carcinoma (51.5%) and this was in accordance with the studies of Goel S et al[26], Tiwari A et al[17], Joshi J et al[22], Dhanalakshmi S et al[23] and Bhat N et al[24]. Few studies like Kedige AR et al[1], Dhar O et al[13], Gundewar M et al[4], Sireesha VJB et al[27] and Tomar V et al[25] were discordant with this study observed adenocarcinoma as the most common histopathological neoplastic finding.

In the present study, the sensitivity of BAL was 18.75%. This was comparable to Tiwari A et al[17] study having 21.57% BAL sensitivity. Many studies, namely Kedige AR et al[1] (100%), Tyagi G et al[16] (43.3%), Ojha PR et al[28] (39%), Chothani K et al[19] (66.67%), Joshi J et al[22] (78.34%), Gundewar M et al[4] (59.2%), Tomar V et al[25] (47.61%), Sareen R et al[21] (72.69%), Bhat N et al[24] (35.5%) and Ahmed A et al[29] (93.44%) showed sensitivity more than that of our study.

BAL was 100% specific in this study and was similar to studies conducted by Chothani K et al[19], Sareen R et al[21] and Ahmed A et al[29]. There were many studies which showed specificity of BAL less than 100% and were discordant with this study. Such studies were Kedige AR et al[1] (88.8%), Tyagi G et al[16] (86.2%), Tiwari A et al[17] (74.21%), Joshi J et al[22] (59.26%), Gundewar M et al[4] (75%), Tomar V et al[25] (75%) and Bhat N et al[24] (78.16%).

In various studies, the diagnostic accuracy varied from 42.23% to 94.52%. the diagnostic accuracy of BAL in this study fell in this range, i.e., 51.85%. It was more than the studies of Tomar V et al[25] and Bhat N et al[24] whereas less than that of the studies of Kedige AR et al[1], Tiwari A et al[17], Chothani K et al[19], Gundewar M et al[4], Sareen R et al[21] and Ahmed A et al[29].

CONCLUSION

This study concluded that -

- It is crucial to be aware of the spectrum of lung lesions for accurate diagnosis as it helps to differentiate benign from malignant lesions, identify early signs of cancer development and helps the clinician to determine the effective management of any disease.
- For diagnosing a lung lesion, it is reasonable to use BAL in suspected cases due to its high specificity because if BAL tests positive, it is highly likely that the disease is present.
- Combined use of cytology and histology gives better results. If further required, IHC will also help in proper subtyping of the malignant lesion.

LIMITATION

There were some hindrances which appeared during this study –

- BAL was less accurate for malignant cases, which could be due to ample amount of inflammation or haemorrhage masking the cells of interest.
- BAL had low sensitivity with respect to histopathological diagnosis due to comparatively higher false negatives, which could be due to sampling error, hypocellular lavage, abundant inflammation and haemorrhage.
- Few malignant cases could not be subtyped properly on cytology. This could be due to low cellularity or inadequate architectural patterns.

RECOMMENDATION

Following are few recommendations in order to overcome the above limitations–

- The sampling error should be minimized by sampling from representative area, taking adequate amount of sample, reducing chances of haemorrhage while performing the procedure and transporting the sample to pathology lab as soon as possible.
- The sample size should be increased in order to get better results.
- A combination of cytological and histological examination should be done in cases where a malignant case could not be subtyped properly on cytology alone.

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