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Panacea Journal of Medical Sciences

Journal homepage: https://pjms.in/

Original Research Article

Histopathological study of lung malignancies on small biopsies - A tertiary care experience in Central India

Ankita Piyush Kolhe[1]*, Amrapali Gaikwad[1], Anjali Bode[1], Rekha Patil[1], Balwant Kowe[1]

[1]Dept. of Pathology, Indira Gandhi Government Medical College Hospital, Nagpur, Maharashtra, India

Abstract

Introduction: Lung cancer accounts for 5.9% of all cancer cases and 8.1% of cancer-related deaths in India**.** In patients with advanced lung malignancies, CT-guided needle biopsy (CTNB) was conducted as they are less invasive and are preferrable to resection to make a pathological diagnosis.

Materials and Methods: Lung malignancies were diagnosed on small biopsies in the Department of Pathology during the period of January 2021 to December 2022, at a tertiary care hospital in state of Maharashtra in India. A retrospective, observational study was conducted on 82 patients with radiologically proven lung malignancies. Amongst 82 cases, 06 cases were inadequate for interpretation and hence excluded from the study. Biopsies were conducted for all cases. Tissue cores of approximate length 1- 1.5 cm were received in 10% formalin in histopathology section which were processed routinely and stained with haematoxylin and eosin stains. Biopsy specimen was considered adequate when it contained more than 20 alveoli.

Results: The histopathological analysis of these specimens showed Adenocarcinoma (36.84%) as the most common lung tumour closely followed by squamous cell carcinoma (34.21%) Subtypes of adenocarcinoma noted included solid pattern (n= 18, 64.29%), acinar pattern (n= 04, 14.29%), mucinous pattern (n= 03, 10.71%) and micropapillary pattern (n= 03, 10.71%). Small cell carcinoma accounted for 15.79% of all cases followed by non-small cell carcinoma (n= 04, 5.26%) adenosquamous carcinoma (n= 03, 3.95%), and metastasis (n= 03, 3.95%).

Conclusion: Due to the advanced nature of presentation and unresectable nature of malignancies in majority of lung cancers, diagnosis of lung tumours heavily relies on small biopsies.

Keywords: Lung malignancy, Adenocarcinoma, Small cell carcinoma

Received: 11-07-2024; **Accepted:** 24-12-2024; **Available Online**: 19-08-2025

1. Introduction

Globally, lung cancer is the most common cancer to be diagnosed and the primary cause of cancer-related mortality. Lung cancer makes up 5.9% of all cancer cases and 8.1% of cancer-related deaths in India.[1]

Indian council of medical research registry predicted 67,000 new cases of of lung cancer by the year 2020 annually rising from 57,795 new cases in 2012.[2]

About 85% of lung cancer patients have symptoms when they first appear. Lung cancer is identified in the remaining cases by a combination of histological analysis and radiographic techniques that were initiated for unrelated medical issues.[3]

In patients with advanced lung malignancies, CT-guided needle biopsy (CTNB) or endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) were conducted as they are less invasive and are preferrable to resection to make a pathological diagnosis.[4]

EBUS TBNA is utilized for the first assessment (i.e., diagnosis, staging, metastasis/recurrence detection) of centrally situated parenchymal lesions detectable with endobronchial ultrasonography, as well as mediastinal and hilar lymph nodes.[5]

Comprehensive molecular characterisation studies in humans have led to the discovery of unique molecular traits in lung cancer, including variations in DNA methylation,

*Corresponding author: Ankita Piyush Kolhe
Email: ankitapkolhe@gmail.com

https://doi.org/10.18231/pjms.v.15.i.2.373-377

mRNA expression, microRNA expression, and protein expression levels, among other subtypes.[6]

This study was conducted to study the relevance of small biopsies in early detection of lung malignancies and classify them according to the latest WHO classification of lung tumours.

2. Aims and objectives

1. To study the relevance of small biopsies in early detection of lung malignancies.
2. To classify small biopsies according to the latest WHO classification of lung tumors.

3. Materials and Methods

Lung malignancies were diagnosed on small biopsies in the Department of Pathology during the period of January 2021 to December 2022, at Indira Gandhi Government Medical College in Nagpur, Maharashtra. A retrospective, observational study was conducted on 82 patients with radiologically proven lung malignancies. Biopsies were conducted for all cases. Tissue cores of approximate length 1- 1.5 cm were received in 10% formalin in histopathology section which were processed routinely and stained with haematoxylin and eosin stains.

Biopsy specimen was considered adequate when it contained more than 20 alveoli. Amongst 82 cases, 06 cases were inadequate for interpretation and hence excluded from the study. The mean age of 55 years was noted in present study with a male to female ratio of 3.4:1.

3.1. Inclusion criteria

1. All biopsy cases of histologically proven malignant lung tumours were included in this study.

3.2. Exclusion criteria

1. Non neoplastic and benign lesions of the lung were excluded from this study.
2. Pleural and mediastinal biopsies were excluded from this study. Resected lung specimens were excluded as well.

4. Results

A total of 82 lung biopsies were analysed from January 2021 to December 2022. Amongst these tumours, 06 samples were insufficient for interpretation.

A suspected lesion on CT scan or X-ray was the commonest indication to perform lung biopsies. The histopathological analysis of these specimens showed Adenocarcinoma (36.84%) as the most common lung tumour closely followed by squamous cell carcinoma (34.21%) Subtypes of adenocarcinoma noted included solid pattern (n= 18, 64.29%), acinar pattern (n= 04, 14.29%), mucinous pattern (n= 03, 10.71%) and micropapillary pattern (n= 03, 10.71%). Small cell carcinoma accounted for 15.79% of all cases followed by non-small cell carcinoma (n= 04, 5.26%) adenosquamous carcinoma (n= 03, 3.95%), and metastasis (n= 03, 3.95%) **(Table 1)**

The mean age of 55 years was noted in present study with a male to female ratio of 3.4:1. **(Table 2)**

Table 1: Malignant lesions in small biopsies

Morphology	Terminology of small biopsies	Frequency (n)	Percentage (%)
Small cell carcinoma	Small cell carcinoma	12	15.79%
Non-small cell carcinoma with neuroendocrine morphology and positive neuroendocrine markers	Large cell carcinoma should be considered	04	5.26%
Squamous cell pattern	Squamous cell carcinoma	26	34.21
Morphological adenocarcinoma pattern	Acinar pattern	04	36.84%
	Solid pattern	18	
	Micropapillary	03	
	Mucinous adenocarcinoma	03	
Morphological presence of both adenocarcinoma and squamous elements	Adenosquamous carcinoma should be considered	03	3.95%
Cases of Metastasis	Metastasis	03	3.95%
Total		76	100

Table 2: Comparative study of lung malignancies in small biopsies

Studies	Mean age	Male to female ratio	Squamous cell carcinoma	Adenocarcinoma	Small cell carcinoma	Other
Current study	55	3.4:1	34.21%	36.84%	15.79%	13.16%
Krishnamurthy et al [7]	56	3.5:1	15.8%	42.6%	13.1%	28.3%
Malik et al [8]	55	4.6:1	25.1%	41%	14.8%	19.1%
Noronha et al [9]	56	3.5:1	24.1%	40.3%	8%	27.6%
Khaparde SH et al[10]	58	3.9:1	26.66%	46.66%	6.66%	20%

5. Discussion

The 2021 update on lung malignancies, mentions that if a diagnosis is rendered on small biopsy specimens, it should be clarified if the diagnosis was made on light microscopy alone or in conjunction with any special stains. Terms such as "Large cell carcinomas" in the diagnosis of small biopsies and cytology specimens are discouraged due to sampling limitations. They also emphasize on the sparing use of "Non-small cell carcinoma" limiting such usage only when a specific diagnosis is not possible.[11]

Due to the advanced nature of presentation and unresectable nature of malignancies in 70% of lung cancers, diagnosis heavily relies on small biopsies.[11]

Detailed classification of lung malignancies on small biopsies were studied in studies conducted by Nicholson et al[11] and in our study as observed in **Table 1**. This table noted the various patterns of adenocarcinoma along with other morphological patterns of other lung malignancies.

During our allocated study period of two years a total of 82 cases of lung malignancies were noted on small biopsies out of which 06 cases were inadequate for interpretation and hence excluded from the study. The most common age group affected were in the 5th to 6th decade. Similar observations were noted in studies conducted by Malik PS et al.[8] However, Khaparde SH et al[10] noted lung malignancies predominantly in 5th-6th decade.

Our study showed a predominance of adenocarcinoma among all malignant small lung biopsies (eighteen cases, 36.84%) These findings were similar to the findings presented by Krishnamurthy et al,[7] Agarwal et al,[2] Sundaram et al.[12] However studies conducted by Kulshrestha R et al,[13] Gupta R et al,[14] Mandal SK et al[15] reported squamous cell carcinoma as the most common lung malignancy.

The male to female ratio was 3.4:1 in present study. Studies conducted by Krishnamurthy et al,[7] Malik et al,[8] Noronha et al,[9] Khaparde SH et al[10] noted male to female ratios of 3.5:1, 4.6:1, 3.5:1 and 3.9:1 respectively as documented in **Table 2**.

5.1. Adenocarcinoma

Twenty eight cases of adenocarcinomas were noted among all malignancies. Subtypes of adenocarcinomas were documented as mucinous, solid, lepidic, papillary and micropapillary. **(Figure 1)**

Invasive mucinous adenocarcinoma on histology present with small, basally oriented nuclei with apical mucin. This subtype is commonly bilateral, multicentric and multilobular.[16]

Lepidic predominant adenocarcinoma is referred to as a tumour of > 3 cm in total size and/or has > 5 mm lymphatic, vascular or pleural invasion with a nonmucinous lepidic predominant growth pattern.[16]

Micropapillary subtype of adenocarcinoma shows small papillary tufts of tumour cells with peripheral nuclei lacking fibrovascular cores.[16]

Following surgical resection, the 5-year survival rate for lepidic predominant adenocarcinoma is an outstanding 90%. Contrasting findings were noted in 81% of non-micropapillary subtypes survival rates five years after surgical excision. Micropapillary subtype of adenocarcinoma noted only 54% survival rates post-surgery.[16]

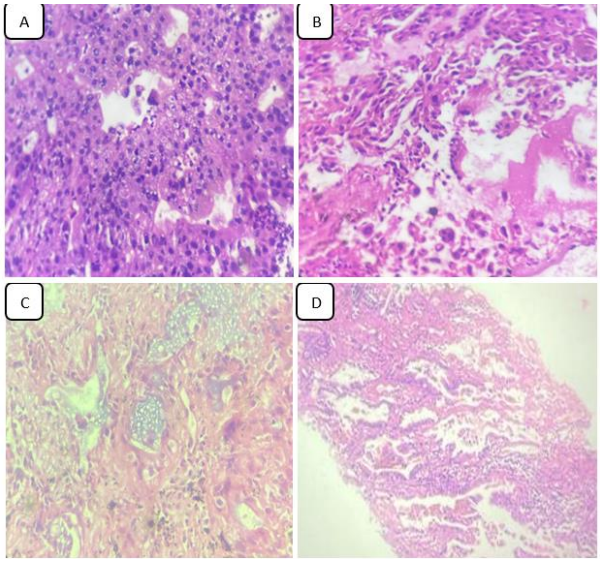

Figure 1: Histological variants of adenocarcinoma; **a:** Solid cell variant (10x); **b:** Micropapillary tufts of tumour cells seen (10x); **c:** Mucinous adenocarcinoma showing pools of mucin (10x); **d:** Lepidic variant (4x).

5.2. Large cell carcinoma

Four cases of non-small cell carcinomas were noted favoring large cell neuroendocrine carcinoma, LCNEC are highly aggressive lung tumors associated with smoking.[17]

Our study reported large cell lung carcinomas to be predominantly noted in the upper lobe of lung in males over 60 years of age. These findings were in accordance with the studies conducted by Cao et al. and Oshiro et al.[17,18]

Histologically, sheets and nests of polygonal cells with moderate- abundant eosinophilic cytoplasm were noted with vesicular nuclear chromatin and prominent nucleoli at places. **(Figure 2)**

On contrast enhanced CT scan, these tumours reveal a well-defined and lobulated appearance without air bronchograms or calcification. Radiological findings were comparable to those of other tumours that were expanding widely, like poorly differentiated adenocarcinomas, squamous cell carcinomas, and peripheral small cell carcinomas.[18]

Most of these tumors are diagnosed at stage III/IV and are treated with combined surgery and chemotherapy.[19] The 5 year survival rate is reported as 30%, worse than other types of NSCC.[20]

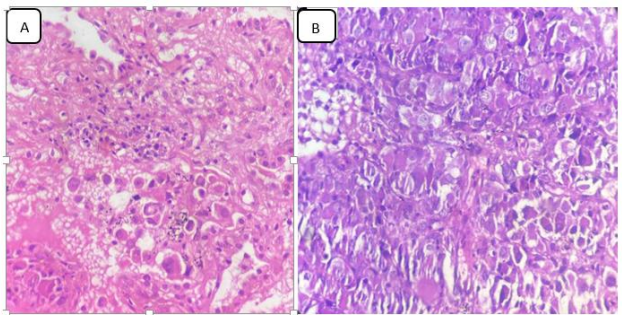

Figure 2: a,b: Non-small cell carcinoma: Histologically shows large polygonal tumour cells in alveolar spaces with abundant eosinophilic cytoplasm separated by stroma.

5.3. Small cell carcinoma

Twelve cases of small cell carcinomas were noted in present study and all cases were associated with smoking. SCLC account for 10% of all lung carcinomas worldwide.[21]

On histology, small cell carcinoma shows sheets of small cells with scant cytoplasm and fine granular nuclear chromatin. Nuclear moulding and crushing artefact are common features. **(Figure 3)**

Extensive intratumoral necrosis is often noted. Immunohistochemistry assays are required for confirmation of diagnosis especially in cases of small biopsies with crushing artefacts.[22]

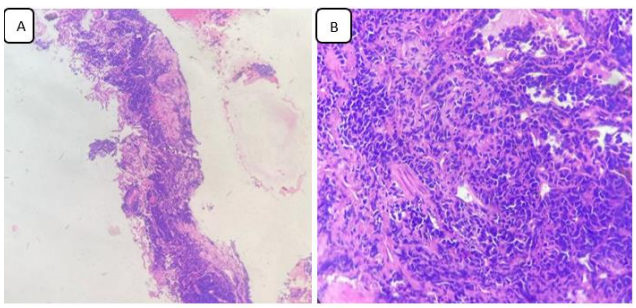

Figure 3: Small cell carcinoma: **a:** Biopsy shows extensive chromatin smearing "crush artefact"4x magnification; **b:** Tightly packed sheets of small cells with scant cytoplasm showing nuclear moulding on 10x magnification

5.4. Adenosquamous carcinoma

Our study revealed three cases of adenosquamous carcinoma. Lung adenosquamous carcinoma (ASC) is a relatively uncommon subtype of non-small cell lung cancer (NSCLC) that accounts for 0.4- 4% of all lung malignancies with male predominance. The glandular and squamous component must account for atleast 20% of the tumour respectively to be considered as adenosquamous carcinoma.[23]

6. Conclusion

Lung cancer is the most common cancer in many nations worldwide to be diagnosed, and it is also one of the leading causes of cancer-related fatalities in both men and women. Poorly differentiated tumours may hamper the precise classification of lung malignancies. A multidisciplinary approach is required for determining the need of lung biopsies in case of lung nodules, masses and pleural etiologies.

In cases of nonspecific diagnoses of tumours, additional information such as differential diagnosis is recommended for appropriate patient management. The current research studied the role of small biopsies in a tertiary care institute in documenting the histomorphological variants of lung carcinoma and grouped the various lung malignancies according to the recent WHO 2021 guidelines.

Further research and molecular studies such as EGFR and KRAS studies are required for categorization due to novel therapeutic and prognostic implications of lung cancers.

7. Ethical approval

This study was conducted after taking approval from the Institute Ethical committee with reference no. IGGMC/Pharmacology/IEC/897-98/2021.

8. Conflict of Interest

None.

9. Source of Funding

None.

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Cite this article: Kolhe AP, Gaikwad A, Bode A, Patil R, Kowe B. Histopathological study of lung malignancies on small biopsies - A tertiary care experience in Central India. *Panacea J Med Sci*. 2025;15(2):373-377.