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Original Research Article

Lung Lesions: Correlation of its Histopathology with Immunohistochemistry

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Abstract:

The anatomical and histological features oblige the Lungs to be most susceptible to invasions. Lung lesions are common due to exposure to various risk factors. A few of themare pollution, smoking, human immunodeficiency virus (HIV), infections, tuberculosis, and malnutrition. An increasing trend in cases of lung cancer is being seen in India. Lung biopsyis a simple, relatively safe, rapid and reliable technique for the diagnosis of pulmonary mass lesions, particularly with the aid of computed tomography (CT) scan. We wanted to study the histopathological pattern of lung lesions along with its distribution with regard to age,sex, and site.

Methods: This is an observational study conducted at the Department of Pathology, ESIC Medical College, Kalaburagi from January 2020 to December 2022. Material for the study consisted of all the biopsies submitted for histopathological and immunohistochemical study.

Results: 164 cases were included in the study, out of which 104 cases (63.41%) were malignant,10 cases (6.10%) were of inflammatory origin and 50 cases (30.49%) showed no evidence of malignancy. Male to Female ratio was 3:1. Most common age group was 51 to 60 years (31.71%). Most common histological type of malignancy was adenocarcinoma (36.54%), followed by squamous cell carcinoma (30.77%).

Conclusions: Lung biopsy is reliable with high accuracy for diagnosis and subtyping of lung lesions. Immunohistochemistry is an important complimentary tool for routine diagnosis of lung cancers.

Keywords: Lung lesions, lung carcinoma, Histopathology

Introduction

The anatomical and histological features oblige the Lungs to be most susceptible to invasions.[1] Lung lesions are common due to exposure to various risk factors.[2] A few of them are pollution, smoking, human immunodeficiency virus (HIV), infections, tuberculosis, and malnutrition.[3] Pulmonary tuberculosis is the most common infectious disease in the world with an estimated one-third of the population infected and 3 million deaths annually.[4,5] In India, the incidence of pulmonary tuberculosis for the year 2021 was 210/100,000.[6] The crude annual incidence of Interstitial lung disease ranges from 1 to 70.1 per 100,000 population in different studies worldwide, while the prevalence lies between 6.27 and 97.9 per 100,000 population.[7] COPD is the second most common pulmonary lesion in India after pulmonary tuberculosis.8 The global burden of Lung Cancer (LC) is increasing. LC represents the rst and third most commonly diagnosed cancer among males and females in 2020, respectively. In 2020, an estimated 2.2 million new LC cases occurred worldwide, representing 14.3% (1.4 million) and 8.4% (0.8 million) of all new cancer diagnoses among males and females, respectively. LC incidence is expected to continue to increase through 2035 in most countries, making LC a major public health challenge worldwide. The ongoing transition in the epidemiology of LC highlights the need for resource redistribution and improved LC control measures to reduce future LC burden worldwide.[9] Lung biopsy is a simple, relatively safe, rapid and reliable technique for the diagnosis of pulmonary mass lesions, particularly with the aid of computed tomography (CT) scan. Lung biopsy (LB) is a standard approach that is used for the safe and reliable diagnosis of nodules and masses present within the lungs [10] Diagnostic tissue biopsies may be obtained through percutaneous route with image-guided needle biopsy or bronchoscopic biopsy for endobronchial lesions or open biopsy if the former modalities could not obtain tissue. TruCut biopsy is a simple procedure, is relatively safe, rapid and a reliable technique for the diagnosis of lung lesions particularly with the aid of a Computed Tomography (CT) scan. Core biopsy not only distinguishes between benign and malignant lesions but also helps in tumour typing and molecular characterization of lung cancers, so customised targeted treatment is possible according to the tumour types.[11]

Although Haematoxylin and Eosin stain is the gold

standard method used for diagnosis, immunohistochemistry (IHC) can enhance the accuracy of such analysis. Immuno histo chemistry can be used in the routine diagnosis of pulmonary tumours in order to identify biological markers (Diagnostic and prognostic) allowing for the earlier initiation of specialised therapies such as chemotherapy or surgery. Immunohistochemistry also helps to increase the accuracy of diagnostic tests.[12] Hence, the present study has been undertaken to correlate the Histopathological findings of lung lesions with its Immunohistochemistry.

Methodology

This observational study was conducted at the Department of Pathology, ESIC Medical College, Kalaburagi from January 2021 to December 2022. We studied all 184 cases oflung biopsies, which were received within 2 years and were subjected to histopathological examination and IHC stain for con rmation whenever required. IHC markers were used when diagnosis cannot be made only by H & E sections. Depending upon a malignant cells pattern and structure on H & E sections, IHC markers were selected and applied and according to results, diagnosis was made.

Statistical analysis

The data analysis was done by descriptive statistics for a percentage of different type of lung lesions and distribute them by age and sex.

Results

In present study of 164 cases of lung biopsy, 104 cases (63.41%) were malignant, 10 cases (6.10%) were of in ammatory conditions, and 50 cases (30.49%) showed no evidence of malignancy. 130 cases (79.27%) were Male and 34 cases (20.73%) were female with male to female ratio of ~4:1. Age ranged from 11 to 80 years with majority of the cases were in the in the age group of 51 to 60 years (52 cases, 31.71%), followed by 61 to 70 years (42 Cases, 25.61%). Out of total 104 malignant cases in this study, 78 (75%) were Male and 26 (25%) were female patients.

According to the histopathological diagnosis, the most common malignant lesion in this study was adenocarcinoma (38 cases, 36.54%), followed by squamous cell carcinoma (32 cases, 30.77%), 8 cases of small cell carcinoma (7.69%), 6 cases of non-small cell carcinoma NOS (5.78%).

Table 1: Histopathological Diagnoses of Malignant Lesions

Diagnosis	Malignant Lesions (n=104)	
	Number	%
Adenocarcinoma	38	36.54%
Adenosquamous Carcinoma	02	1.92%
Carcinoid tumor	02	1.92%
Lymphoblastic lymphoma	04	3.85%
Non-small cell carcinoma	04	3.85%
Poorly differentiated adenocarcinoma	02	1.92%
Non-small cell lung carcinoma, NOS	06	5.78%
Poorly differentiated squamouscell carcinoma	02	1.92%
Small cell carcinoma	08	7.69%
Small cell neuroendocrine Tumor	02	1.92%
Squamous cell carcinoma	32	30.77%
Synovial sarcoma	02	1.92%
Total	104	100%

In males, there were 30 cases of adenocarcinoma (38.47%) and 30 cases of squamous cell carcinoma (38.47%), followed by 4 cases of non-small cell lung carcinoma, NOS (5.13%). In females, adenocarcinoma was seen in 8 cases (30.58%) among the other carcinoma detected. Out of 10 cases of inflammatory lesions, two cases were of nonspecific in animation, the other 6 were of granulomatous inflammation, tuberculous inflammation, and desquamative interstitial pneumonia. In present study, immunohistochemistry was applied in 76 cases. With the use of IHC markers, diagnosis of adenocarcinoma, squamous cell carcinoma, adenosquamous carcinoma, lymphoblastic lymphoma, carcinoid tumor, non-small cell lung carcinoma, NOS, poorly differentiated squamous cell carcinoma, small cell carcinoma, and synovial sarcoma have been confirmed.

Table 2: Results of IHC Markers in DifferentHistologicalTypes of Lung Cancer

	Diagnosis	IHC Markers	
		Positive	Negative
1.	Adenocarcino Ma	CK7TTF-1	CK5/6, p63
2.	Squamouscell carcinoma	CK5/6, p63	CK7, TTF-1
3.	Adenosquamous carcinoma	CK5/6, p63 (in squamoidareas), CK7 (in glandular areas)	-
4.	Carcinoidtumor	Pan-keratin, Synaptophysin,Chromogranin	-
5.	Lymphoblastic lymphoma	CD99, CD2,CD5, LCA, CD20, Pankeratin,	CD1a, S100, Synaptophysin, Chromogranin

6.	Poorly differentiated squamous cellcarcinoma	CK5/6	P63, Synaptophysin,Chromogranin
7.	Non-small cell, lung carcinoma, NOS	Pankeratin	P63, CK5/6,CK7, Synaptophysin, Chromogranin
8.	Small cellcarcinoma	Synaptophysin,Chromogranin	
9.	Synovialsarcoma	BCL-2, CD99	S100, Calretinin

Discussion

Lung biopsy is widely recognized as a valuable tool for the diagnosis and management of diverse pulmonary disorders. Trans bronchial lung biopsy, open lung biopsy, and CT guided core needle biopsy are the principal tools that have been developed for obtaining lung tissue for histopathological examination.[11,12] CT-guided percutaneous needle biopsy of the lung is commonly used as an outpatient diagnostic procedure and is relatively safe, sensitive and accurate method of diagnosing benign and malignant lesions as well as suitable for obtaining tissue samples of sufficient quantity and quality for allowing molecular analysis of biomarkers. Image-guided approaches also allow biopsy from areas of the tumor felt most likely to harbor viable tumor (i.e., avoiding centrally necrotic areas) and representative of whole tumor. TruCut biopsy is very helpful in early diagnosis and less invasive as compared to excision especially to differentiate benign from malignant tumor and when oncosurgeon is planning pre- operative chemotherapy or in advanced disease and in small cell carcinoma where surgery is not recommended.[11,12] The incidence rate of malignant lesions in the present study (63.41%) was similar to the study of Kinnari S. Naik et al [13] (75.6%) and Pradeep Kumar Giri et al [14] (75%). The incidence rate of inflammatory conditions was 6.10% in the present study as compared to 15.4% and 22.5% in the study of Kinnari S. Naik et al [13] and Pradeep Kumar Giri et al [14] respectively. The male to female ratio in present study was ~4:1, while it was contradictory to Kinnari S. Naik et al13 study (2:1), Pradeep Kumar Giri et al14study (2.75:1). In the present study, maximum malignant cases were seen in the age group of 61 to 70 years, which was similar to Anjan Das et al [15] study. The incidence rate was 25% in the age group of 51 to 60 years in the present study which almost similar to Pradeep Kumar Giri et al14study, which was 20%.Present study and study by Pradeep Kumar Giri et al [14], Kinnari S. Naik et al [13] and Deependra K Rai et al [16] showed similar result with predominance of adenocarcinoma followed by squamous cell carcinoma and small cell carcinoma. The incidence rate of adenocarcinoma (36.54%) and squamous cell carcinoma (30.77%) in the present study were almost similar to Kinnari S. Naik et al [13] study with the incidence rate of 38% and 22.4% respectively.

When comparing the characteristics of the lung cancer cases, squamous cell carcinoma was the predominant type of lung cancer among men but women were found to be more likely to have adenocarcinoma as compared to men and this was consistent with Kinnari S. Naik et al [13] and Kumar et al.[17] The incidence of tuberculous in ammation was almost similar in the study of Pradeep Kumar Giri et al [14] (11.1%) and present study (20%). In an era of precision medicine, immunohistochemistry plays a critical role in the classification of tumors into subtypes and for assessing biomarkers for timely and accurate therapeutic decision-making. Compared with other techniques, immuno histochemistry has a number of advantages, including being widely available, technically less challenging, and cost- ef cient with a rapid turn-around time. Thus, molecular specic immunohistochemical assays have huge potential as practical screening tools for the detection of druggable genetic alterations and for the assessment of biomarkers for molecular- targeted therapy. In addition, immunohistohemistry can be interpreted using fewer tumor cells than are required for other molecular techniques. Moreover, immunohistochemistry allows for the evaluation of cellular localization and staining patterns in the context of tumor structures; thus, a greater range of information is provided. In present study, immunohistochemistry was performed in total 76 cases. Out of 38 cases of adenocarcinoma, IHC was performed in 30 cases for confirmation of diagnosis. Rest of 8 cases were diagnosed on H & E sections. IHC markers, that have been applied were, CK7, TTF-1, CK5/6, and p63. All the 30 cases were positive for CK7 and TTF-1 whereas negative for CK5/6 and p63. These results showed concordance with Kinnari S. Naik et al [13] other. Out of 32 cases of squamous cell carcinoma, 8 cases were diagnosed on H & E sections and rest of 24 cases were con rmed by immunohistochemistry. IHC markers, that have been applied were, p63, CK5/6, CK7, and TTF-1. All the cases were positive for CK5/6 and p63 whereas negative for CK7 and TTF-1. These results showed concordance with Kinnari S. Naik et al.[13] A case of adenosquamous carcinoma was con rmed by using CK7, p63, and CK5/6. CK7 was positive in glandular areas whereas CK5/6 and p63 were positive in squamoid areas. In the case of lymphoblastic lymphoma, microscopically, there was a monomorphic population of atypical lymphoid cells with fine nuclear chromatin and convoluted nucleus. IHC markers, CD2, CD5, CD99, CD20, CD1a, LCA, S100, Synaptophysin, and chromogranin were applied. Out of which, CD2, CD5, CD20, CD99, and LCA were positive. So according to this result lymphoblastic lymphoma diagnosis was given. In a case of carcinoid tumor, microscopically, tumor cells were monomorphic, hyper chromatic showing finely granular chromatin and eosinophilic cytoplasm. IHC markers synaptophysin, chromogranin, and pankeratin were applied for confirmation. All markers were positive. In case of non-small cell lung carcinoma, NOS type, microscopically tumour cells were hyper chromatic showing indistinct cell border and moderate cytoplasm. IHC

markers P63, CK5/6, CK7, synaptophysin, chromogranin, and pankeratin were applied for subtyping of non-small cell carcinoma. Only pankeratin was positive, so non-small cell lung carcinoma, NOS diagnosis was given. Poorly differentiated squamous cell carcinoma was confirmed by applying IHC markers, CK5/6, p63, synaptophysin and chromogranin. Only CK5/6 was positive and other markers were negative. Out of 8 cases of small cell carcinoma, one case was diagnosed on H & E sections. Other cases were confirmed by using IHC markers, synaptophysin and chromogranin. These markers were positive in all three cases. In a case of synovial sarcoma, microscopically tumour was composed of solid sheets of round to spindle cells with intervening hemangiopericytoma-like vessels. Cells were hyper chromatic and having high nuclear to cytoplasmic ratio. BCL-2, CD99, S100, and calretinin IHC markers were applied for confirmation. BCL-2 and CD99 were positive.

Conclusion

Lung biopsy is reliable with high accuracy for diagnosis and subtyping of lung lesions. Histopathological examination plays an important role in making an accurate diagnosis of various lesions of lung. Although Haematoxylin and Eosin stain is the gold standard method used for diagnosis, immunohistochemistry is an important complimentary tool for routine diagnosis of lung cancers.

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