Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL 14, ISSUE 07, 2023

Original Research Article

TO STUDY THE EXPRESSION OF P63 IN DIFFERENT HISTOLOGIC TYPES OF LUNGCARCINOMAS

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Article History: **Received:** 11.07.2023 **Revised:**19.07.2023 **Accepted:** 26.07.2023

Abstract

Lung cancer ranks among the most common and most lethal malignancies worldwide. It is rapidly emerging as a major cause of mortality in the Middle East, Africa, and Asia as well; and is increasingly being recognizedin India

Materials and methods: A total of 105 fibreoptic lung biopsy specimens were received in the Department of Pathology, VTSM Peripheral Cancer Centre (Branch Of Kidwai Cancer Institute ,Bangalore

Results: Age range of patients undergoing fibreoptic lung biopsies was from 21to 85. The age range of squamous cell carcinoma was from 35 to 85 andadenocarcinoma was from 45 to 75.

Conclusion: Lung carcinomas had a peak incidence in the group 40 to 70 years ofage and was more common in males than in females. Most common clinical presentations were found to be cough, breathlessness and weight loss.

Keywords: Lung,Carcinoma,p53

Introduction

Lung cancer ranks among the most common and most lethal malignancies worldwide. It is rapidly emerging as a major cause of mortality in the Middle East, Africa, and Asia as well; and is increasingly being recognizedin India[2]. Death rates attributable to this disease are expected to increase substantially over the next several decades[3].

Procedures used to diagnose bronchopulmonary neoplasms should be as accurate as possible and should provide optimum characterization of the tumor type. Fibreoptic bronchoscopic biopsy refers to the bronchoscopic technique of obtaining pulmonary parenchymal tissue for histological analysis. It is one of the common modality used to diagnose lung cancer and is the best technique for obtaining specimens to diagnose endobronchial lung carcinoma. The lesion can be visualized and the location of the specimen can be mapped preciselywith a fibreoptic bronchoscope.

The histopathologic distinction of small cell from non–small cell carcinoma of lung is important therapeutically. However, such distinction may not always be straightforward based

ISSN: 0975-3583, 0976-2833 VOL 14, ISSUE 07, 2023

on morphologic findings alone, especiallyin cytologic specimens, but in tissue specimens as well.

p63 is a recently discovered member of the p53 family that has been shown to be important in the development of epithelial tissues. p63 may also play a role in squamous cell carcinomas of the lung, head and neck, and cervix, and its expression is increased in these tumors[1]. The purpose of this study was to analyse the demographics, risk factors, distribution of lung carcinomas and to investigate the expression of p63 in various histologic types of lung tumors and correlate with histological gradings.

MATERIALS AND METHODS

A total of 105 fibreoptic lung biopsy specimens were received in the Department of Pathology, VTSM Peripheral Cancer Centre (Branch Of Kidwai Cancer Institute ,Bangalore

Inclusion Criteria

All patients undergoing fibreoptic endoscopic biopsies, irrespective ofage and sex were included for the study

Exclusion Criteria

Patients with inadequate biopsy material were excluded from the study.

RESULTS

A total of 96 cases were studied. Morphology showed the followingresults.

NORMAL	45
NON NEOPLASTIC LESIONS	22
Non specific inflammation	8
Chronic inflammation	9
Granulomatous lesion	3
Other infections (candidiasis, aspergillosis)	2
PRE NEOPLASTIC LESIONS	6
Mild dysplasia (fig. 1,2)	2
Moderate dysplasia(fig. 3,4)	3
Severe dysplasia(fig. 5,6)	1
NEOPLASTIC LESIONS	23
Squamous cell carcinoma(fig. 7,8,9,10)	12
Adenocarcinoma(fig. 11,12)	8
Bronchioloalveolar carcinoma (mucinous type)	1
Bronchioloalveolar carcinoma (non mucinous type)	1
Large cell carcinoma	1

AGE AND SEX DISTRIBUTION OF PATIENTS UNDERGOINGFIBREOPTIC LUNG BIOPSY

TABLE NO 1

Age	Non Malignant			Pre Malignant			Malignant			Total		
	M	F	T	M	F	T	M	F	T	M	F	T
21 TO 30	4	4	8	0	0	0	0	0	0	4	4	8

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31 TO 40	7	3	10	0	0	0	2	0	2	9	3	12
41 TO 50	19	1	20	2	0	2	6	1	7	27	2	29
51 TO 60	20	1	21	1	0	1	5	0	5	26	1	27
61 TO 70	8	5	13	2	0	2	6	1	7	16	6	22
71 TO 80	2	2	4	1	0	1	0	1	1	3	3	6
81 TO 90	0	0	0	0	0	0	1	0	1	1	0	1
TOTAL	60	16	76	6	0	6	20	3	23	86	19	105

AGE AND SEX DISTRIBUTION OF LUNG MALIGNANCIESTABLE NO 2

Age	**Squamous Cell Carcinoma**			**Adeno Carcinoma**			**Others**			**Total**		
	M	**F**	**T**	**M**	**F**	**T**	**M**	**F**	**T**	**M**	**F**	**T**
21 TO 30	0	0	0	0	0	0	0	0	0	0	0	0
31 TO 40	2	0	2	0	0	0	0	0	0	2	0	2
41 TO 50	3	0	3	2	0	2	1	1	2	6	1	7
51 TO 60	2	0	2	2	0	2	1	0	1	5	0	5
61 TO 70	4	0	4	2	1	3	0	0	0	6	1	7
71 TO 80	0	0	0	0	1	1	0	0	0	0	1	1
81 TO 90	1	0	1	0	0	0	0	0	0	1	0	1
TOTAL	12	0	12	6	2	8	2	1	3	20	3	23

Age range of patients undergoing fibreoptic lung biopsies was from 21to 85. The age range of squamous cell carcinoma was from 35 to 85 andadenocarcinoma was from 45 to 75.

Both squamous and adenocarcinomas occurred in males predominantly.

CLINICAL PRESENTATION OF LUNG MALIGNANCIES SQUAMOUS CELL CARCINOMA

TABLE NO 3

CLINICAL PRESENTATION	**NO OFCASES**	**%**
COUGH	7	58.33%
HEMOPTYSIS	4	33.33%
BREATHLESSNESS	10	83.33%
LOSS OF WEIGHT	11	91.67%
CHEST PAIN	6	50%

ADENOCARCINOMATABLE NO 4

CLINICAL PRESENTATION	**NO OFCASES**	**%**
COUGH	6	75%
HEMOPTYSIS	0	0%
BREATHLESSNESS	5	62.50%

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LOSS OF WEIGHT	8	100%
CHEST PAIN	3	37.50%

Cough, breathlessness and weight loss were the most common clinicalpresentation of both squamous and adenocarcinoma.

ASSOCIATION OF MALIGNANCIES WITH SMOKING

SMOKING ASSOCIATION IN NON MALIGNANT AND MALIGNANTLESIONS

TABLE NO 5

	H/O SMOKING	**NO H/O SMOKING**	**TOTAL**
MALIGNANTLESIONS	17	12	29
NON MALIGNANTLESIONS	42	34	76
TOTAL	57	48	

Yates corrected chi square – 0.0081; p value – 0.9282(not significant)

SMOKING ASSOCIATION IN SQUAMOUS AND NON SQUAMOUSMALIGNANCIES

TABLE NO 6

	H/O SMOKING	**NO H/O SMOKING**	**TOTAL**
SQUAMOUS CELL CARCINOMAS	9	3	12
NONSQUAMOUS CELL CARCINOMAS	3	8	11
TOTAL	12	11	

Yates corrected chi square – 3.5010; p value – 0.0613(not significant).
Squamous cell carcinomas were most commonly associated with history of smoking which is statistically insignificant probably due to reduced sample size.

IMAGING FINDINGS SQUAMOUS CELL CARCINOMATABLE NO 7

XRAY FINDINGS	**NO OF CASES**	**%**
HILAR MASS	5	41.65%
CONSOLIDATION	3	25%
OPACITY	1	8.33%
CAVITY	1	8.33%

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RIB METASTASIS	1	8.33%
NORMAL	1	8.33%

ADENOCARCINOMATABLE NO 8

XRAY FINDINGS	NO OF CASES	%
OPACITY	5	62.50%
CONSOLIDATION	1	12.50%
HILAR PROMINANCE	1	12.50%
PLEURAL EFFUSION	1	12.50%

Most common x ray finding of squamous cell carcinomas was found tobe hilar mass. Other less common findings are consolidation, opacity and cavity formation. Most common x ray finding of adenocarcinomas was foundto be opacity. Other less common findings are consolidation, hilar prominence, pleural effusion.

FIBREOPTIC BRONCHOSCOPIC FINDINGSSQUAMOUS CELL CARCINOMA

TABLE NO 9

FOB FINDINGS	NO OF CASES	%
GROWTH	10	83.33%
UNHEALTHYMUCOSA	1	8.33%
NECROTICMATERIAL	1	8.33%

ADENOCARCINOMATABLE NO 10

FOB FINDINGS	NO OF CASES	%
GROWTH	6	75%
NARROWING OFBRONCHUS	2	25%

Most of the carcinomas (squamous and adeno) presented withendobronchial growth at fibreoptic bronchoscopy.

DISCUSSION

Lung cancer is the most common fatal malignancy in men and women. Lung cancer has a peak incidence in the group 50 to 70 years of age[4] whereas in this study, the age range of lung malignancies was found to be 35 to 85 and peak incidence was around 40 to 70 years of age. Lung cancer is more common in males than in females. In this study also it is more common inmales. This may be due to less use of medical services by females in our population[5].

Local and systemic symptoms of most lung cancers are related to mass effect of the tumor. Local symptoms include cough, hemoptysis, dyspnoea and chest pain. Systemic symptoms include weight loss, cachexia and pain attributable to metastases[6]. In concordance with

ISSN: 0975-3583, 0976-2833 VOL 14, ISSUE 07, 2023

literature, the most common clinical presentations in this study were found to be cough, breathlessness and weight loss.

All cell types of lung cancer are associated with smoking. The strongest associations are with small cell and squamous cell carcinomas[8]. Similarly, in this study, squamous cell carcinomas were found to be most commonlyassociated with history of smoking.

Performing a chest radiograph is the first step if a patient reports with symptoms that may suggest lung cancer. This may reveal an obvious mass, widening of the mediastinum (suggestive of spread to lymph nodes there),
atelectasis (collapse), consolidation (pneumonia), opacity, cavity, pleural effusion[7]. Accordingly, in this study, the most common x ray findings were found to be hilar mass, opacity and consolidation.

Tissue needs to be obtained to confirm the diagnosis of lung cancer. Flexible bronchoscopy is an invasive, nonsurgical approach used to obtain tissue. Flexible bronchoscopy has a high diagnostic yield for endoscopically visible lesions. Most common findings at fibreoptic bronchoscopy were growth, purulent secretions, inflamed mucosa and necrotic material[9]. In this study also, the most common findings at fibreoptic bronchoscopy were growth, unhealthy mucosa, necrotic material and narrowing of bronchus.

The incidence of lung cancer seems to be on increase in Asia and many other parts of the world and currently death caused by lung cancer is the leading cause of neoplasia related mortality world wide[10]. This may be dueto lack of early detection strategies in diagnosis of lung tumors. Genomic abnormalities may play a major role in malignant transformation and tumor progression[11].

p63 is a transcription factor that transactivates p53 target genes [12] and induces apoptosis when expressed in cells [13]. Although p63 was recentlydiscovered, it is the most ancient member of the p53 family [14].

p63 genomic sequence is found in chromosome 3q27. Chromosome 3q26-ter amplification, which includes the *p63* gene locus, is one of the most
prevalent genomic abnormalities in solid tumors and is likely to play a critical role in tumorigenesis. Amplification of chromosome 3q has been described in squamous epithelial transformation from the lung [15], head and neck [16,17], esophagus [18], bladder [19], cervix [20,21], and stomach [22]. It is demonstrated that the presence of 3q amplification alone allows the distinction between squamous and adenocarcinoma in more than 75% of cases [23].

p63 functions as a potent transcriptional repressor and dissociates from promoter binding sites of key growth inhibitory genes during normal human keratinocyte differentiation[15]. Thus, *p63* gene overexpression may have important implications in lung tumorigenesis.

CONCLUSION

96 adequate samples of fibreoptic lung biopsy specimens received for the study. Demographic and risk factor analysis of the cases were done. Histopathological examination of all the cases was done. Immnohistochemical analysis of p63 antibody was done. Lung carcinomas had a peak incidence in the group 40 to 70 years ofage and was more common in males than in females. Most common clinical presentations were found to be cough,

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breathlessness and weight loss.Squamous cell carcinomas were found to be most commonly associated with history of smoking. The most common X ray findings were found to be mass lesion, opacity and consolidation. The most common findings at fibreoptic bronchoscopy were growth, unhealthy mucosa, necrotic material and narrowing of bronchus.