Histopathological Patterns of Endobronchial Lung Biopsy Specimen in Lung Cancer along with Clinico - Radiological Correlation

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ABSTRACT

Introduction: Lung cancer is one of the commonest lethal cancers known till date. Along with the typical symptomatic clinical presentation, it is appropriately detected by various radiographic evaluation methods sometimes initiated for an unrelated problem. Great interest has now been developed in the histological characterisation of lung cancer in view of newer histology guided therapeutic modalities and genomic classification of lung carcinoma. Study aimed to explore histopathological patterns of lung cancer in relation to clinico-radiological features.

Material and Methods: This prospective study was conducted on 80 patients of suspected lung cancer over a period of one year, to study clinical features, radiological manifestations and histological types of lung cancer. The study was done following a standard study protocol which included a clinical history regarding the onset and progress of the disease, smoking habits, detailed physical examination of the respiratory system, chest roentgenogram, computed tomography of thorax, fiberoptic bronchoscopy and others.

Results: Patients mean age was 59.9 years, 83.7% males and 16.3% females. The smoker to non-smoker ratio was 7.8:1. Cough was the most common presenting symptom (87.5%). The most common radiological finding was mass lesion (87.5%), followed by collapse consolidation in 36.25%. Squamous cell carcinoma presented more commonly as hilar mass (57.5%), while adenocarcinoma as peripheral mass lesion (66.7%). The most common finding on histopathological examination was Squamous cell carcinoma (50%), followed by small cell carcinoma (15%) and adenocarcinoma (3.75%).

Conclusion: Endobronchial lung biopsy and histopathological examination is an extremely useful method for establishing diagnosis of lung cancer in patients suspected to have malignancy by clinical or radiological criteria.

Keywords: Lung Cancer, Radiological Patterns, Histopathological Types

INTRODUCTION

Lung cancer is most common and serious health problem worldwide. All over world it accounts for 13% of all new cancer cases and 19% of cancer related deaths.[1] Majority of patients having lung cancer had direct exposure to smoking. Squamous cell carcinomas and small cell carcinomas shows significant association with smoking.[2] Occupational exposures and air pollution approximately accounts for 2% to 9% of lung cancers. Approximately 85% patients with lung cancer are symptomatic at presentation. In remaining patients, lung cancer is diagnosed by various radiological methods initiated for an unrelated health problem and histopathological examination.[3]

The clinical features of carcinoma lung result from the local growth and regional growth of the tumor as well as lymphatic invasion, haematogenous distant metastatic spread and remote para-neoplastic effects from tumour products or immune cross- reaction with tumour antigens.[4] More interest has been developed in the histological characterisation of lung cancer in recent years in view of newer histology guided therapeutic modalities and genomic classification of lung carcinoma.[5-6] At present more than 50% of lung adenocarcinomas and about a third of squamous cell carcinomas can be characterised based on the mutation profile. Epidermal growth factor receptors (EGFR) mutation explain the therapeutic importance of molecular classification.[7] The present study explored histopathological patterns of lung cancer in relation to clinico-radiological features.

MATERIAL AND METHODS

This prospective study was an observational study conducted in the histopathology section of the Department of Pathology in collaboration with Chest Diseases Hospital Government Medical College, Jammu over a period of one year.

Study material included all endobronchial lung biopsy specimen received in the histopathology section of Department of Pathology.

Detailed medical history of the patient regarding the onset and progression of the disease and smoking habits and other risk factors was taken. The patients were thoroughly examined for general physical examination with a detailed clinical examination of the respiratory system. Suspected lung cancer cases were subjected to radiological evaluation. Radiological findings were evaluated based on distribution, location, number and involvement of adjacent structures if any. All the biopsy specimen submitted were grossed meticulously and after proper tissue processing sections

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Chief complaints	Male (n=67)		Female (n=13)		Total (n=80)	
	No.	%	No.	%	No.	%
Cough	58	86.56	12	92.30	70	87.5
Fever	16	23.88	2	15.38	18	22.5
Expectoration	15	22.38	1	7.69	16	20
Haemoptysis	23	34.32	5	38.46	28	35
Breathlessness	25	37.31	3	23.07	28	35
Chest pain	33	49.25	4	30.76	37	46.25
Loss of weight/Loss of appetite	5	7.46	0	0	5	6.25
Hoarseness of voice	4	5.97	0	0	4	5
K/c/o CA lung	1	1.49	0	0	1	1.25
Table-1: Chief presenting complaints						

	Squamous cell carcinoma No. (%)	Small cell carcinoma No. (%)	Adenocarcinoma No. (%)	Total No. (%)
No. of patients	40 (72.7)	12 (21.8)	3 (5.5)	55 (100)
Site of tumours				
Right lung	31 (77.5)	5 (41.7)	1 (33.3)	37 (67.3)
Left lung	7 (17.5)	7 (58.3)	2 (66.7)	16 (29.1)
Bilateral	2 (5)	0	0	2 (3.6)
Location				
Hilar	23 (57.5)	5 (41.7)	1 (33.3)	29 (52.7)
Upper zone	7 (17.5)	3 (25)	2 (66.7)	12 (21.8)
Mid zone	4 (10)	1 (8.3)	0	5 (9.1)
Lower zone	6 (15)	3 (25)	0	9 (16.4)
Lesions				
Mass lesion	26 (65)	10 (83.3)	1 (33.3)	37 (67.3)
Collapse	7 (17.5)	2 (16.7)	2 (66.7)	11 (20)
Combinations	7 (17.5)	0	0	7 (12.7)
Associated Pleural effusion	10 (25)	0	2 (16.7)	12 (21.8)
Special features				
Metastasis	5 (12.5)	0	0	5 (9.1)
Table-2: Radiological findings in the various histologic types of lung cancer patients				

CECT findings	Total (n=80)	
	No.	%
Hilar mass	30	37.5
Right lung mass	29	36.25
Collapse/Consolidation	29	36.25
Mediastinal LAP	28	35
Pleural effusion	16	20
Left lung mass	11	13.75
Hilar LAP	11	13.75
Metastasis	5	6.25
Table-3: CECT Findings		

Bronchoscopy Findings	Total(n=80)	
	No.	%
Endobronchial mass lesion	68	85
Narrowing of bronchus	1	1.25
Vocal cord paralysis	4	5
No EB lesion	7	8.75
Table-4: Fiberoptic bronchoscopy findings		

of 4-5 micron thickness were prepared from the specimen submitted. The sections were stained routinely with H & E. Staining procedures were done as described by Bancroft and Stevens (2002). The histopathological patterns were based on the WHO classification of lung tumours.[8]

STATISTICAL ANALYSIS

Statistical analysis was done using SPSS of latest version wherever required. Descriptive statistics like mean and percentages were done to interpret the data.

RESULTS

A total of 80 patients suspected of lung cancer were studied. The mean age of the patients was 59.9 (range 24-85 years) years. Only 5 (6.25%) patients were below the age of 40 years, youngest being 24 years old. Majority of the cases, 67 (83.75%) were between 50 to 80 years. Out of 80 cases, 67 (83.7%) were males and 13 (16.3%) were females. Male to female ratio was 5.15:1. Seventy one (88.75%) patients were smokers. The smoker to non-smoker ratio was 7.8:1. Most common presenting symptom was cough in 70 (87.5%) cases followed by chest pain in 37 (46.25%) cases(Table 1). Three (3.75%) out of 80 patients had a history of anti-tubercular treatment.

Right lung was most commonly involved 37 (67.3%) followed by hilar region involved in 29 (52.7%) cases. Upper zone was involved in 12 (21.8%) cases, lower zone in 9 (16.4%) cases and mid zone in 5 (9.1%) cases. Mass

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Histologic diagnosis	Male(n=67)		Female(n=13)		Total (n=80)	
	No.	%	No.	%	No.	%
Squamous Cell Ca	35	52.28	5	38.46	40	50
Small Cell Ca	12	17.91	-	-	12	15
Adenocarcinoma	2	2.98	1	7.69	3	3.75
Mod to severe Dysplasia	2	2.98	-	-	2	2.5
Granulomatous inflammation	1	1.49	1	7.69	2	2.5
Non-specific inflammation	7	10.44	3	23.07	10	12.5
Inadequate biopsy	8	11.94	3	23.07	11	13.75
Table-5: Histologic diagnosis						

Authors	Total	M:F	Age (yr)	Sm/NS	Squamous Cell Ca	Small Cell Ca	Adeno Ca	Unclassified
Koul PA 2010[30]	462	6.1:1	57.6	4.6:1	67.5	20.8	3.03	4.7
Agarwal JP et al 2012[28]	489	3.5:1	56	0.91:1	26.2	8	43.8	-
Dey A et al 2012[11]	607	4.14:1	57.9	2.5:1	35.1	16.5	30.8	11.7
Mandal SK et al 2013[10]	466	1.09:1	60	3.7:1	49.1	14.8	30.8	1.5
Agarwala A et al 2014[20]	160	7:1	-	7.8:1	51.25	11.25	31.25	-
Prasad R et al 2015[29]	124	-	61	0.06:1	33.1	23.4	43.5	-
Dubey N et al 2015[14]	47	4.2:1	58.6	3.7:1	38.2	6.3	31.9	-
Pandhi N et al 2015[12]	150	2.7:1	59.3	1.5:1	41	13	36	-
Gupta R et al 2015[17]	170	6.39:1	55.94	3.9:1	45.3	10.6	35.3	-
Dhandapani S et al 2016[27]	54	3.9:1	59.8	1.45:1	35.18	5.6	42.6	16.7
Kumar et al 2016[21]	110	5.6:1	58.6	4.5:1	32.7	20.0	40.9	-
Present study	80	5.15:1	58.21	7.8:1	50	15	3.75	-
Table-6: Comparative clinical features and cell type patterns as reported in different Indian studies								

lesion was the most common radiological finding in 37 (67.3%) cases followed by collapse in 11 (20%) cases. Combined presentation was observed in 7 (12.72%). Pleural effusion was observed in 12 (21.8%) cases, most of them having squamous cell carcinoma. Evidence of metastasis to liver, bone, adrenal, ipsilateral chest wall and pulmonary metastasis was present in 5 (9.1%) cases all of which had squamous cell carcinoma (Table 2).

CT thorax was done in all patients. Mass lesion was detected in 70 (87.5%) patients. Mediastinal lymphadenopathy was detected in 28 (35%). Hilar lymphadenopathy was seen in 11 (13.75%) patients. Metastasis was seen in 5 (6.25%) patients (Table 3).

Endobronchial mass lesion was most common bronchoscopic finding seen in 68 (85%) patients. Vocal cord paralysis was seen in 4 (5%) patients (Table 4).

Squamous cell carcinoma was found to be the most common type of carcinoma lung and was found in 40 (50%) patients, followed by small cell carcinoma which was present in 12 (15%) patients (Table 5).

The most common cell type was squamous cell carcinoma (72.72%), followed by small cell carcinoma (21.81%). Commonest histological subtype amongst smokers was squamous cell carcinoma 35 cases (69.63%), followed by small cell carcinoma 12 cases (21.81%). Amongst non-smokers also (i.e 5 cases) the commonest pathological diagnosis was squamous cell carcinoma.

DISCUSSION

Now a days, majority of cancer deaths are due to lung cancer.[9] Endobronchial lung biopsy is an effective and less invasive procedure useful for diagnosis of lung cancer. In this study the mean age of lung carcinoma patients were 59.9 years. This showed that lung cancer mostly occur in older age. Age group in the present study is comparable to the study conducted by Mandal et al.[10] which show that age ranged between 39 to 85 years. The average age of the lung cancer patients in the present study is also comparable to some of Indian studies.[11-13] The sex ratio reported in various Indian studies ranged from 4.2:1 to 7:1.[14-17] The sex ratio in our study was 5.15:1. Male predominates in the present study. This showed that in India, females have still lower prevalence of smoking. In our study, 95.52% males were smokers and only 4.48% were non-smokers. This is similar with the survey conducted by WHO in 1986 in which 92-94% lung cancer deaths were attributed to tobacco smoking in males. The smoker to non-smoker ratio in our study was 7.8:1 which is comparable with the study by Rawat et al.[18] and Khan et al.[19] In the present study, the commonest symptom was cough present in 87.5% patients. This is comparable to various other studies.[17,20,21] Chest pain was present in 46.25% patients in over study. This is also comparable to various studies.[20-21] Various studies have reported haemoptysis in 11% to 24% lung cancer patients.[12,18] A higher percentage of haemoptysis (69.2%) have reported in study conducted by Jindal and Behera.[22] In the present study haemoptysis was present in 35% patients. One important observation is that, 3.75% of the cases in our study were misdiagnosed as tuberculosis and treated at various other centres, thereby causing a delay in diagnosis and time of presentation. Rawat et al.[18] reported delay in presentation of patients

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to their attending physician. Majority of the cases were misdiagnosed as tuberculosis and treated at various other centres, thereby causing a delay in seeking treatment which varied from 4-6 months. Dubey et al.[14] also reported 23.4% cases of lung malignancy which had been misdiagnosed as pulmonary tuberculosis. Radiographic analysis of patients with lung cancer in various published studies has revealed a preponderance of right lung involvement with upper lobe as the commonest site of involvement.[10,17,23] This was noticed in the present study also. It is well known that squamous cell carcinoma presents mostly as a central tumour. In this study 57.5% of squamous cell carcinoma had hilar mass. This is comparable with the study conducted by Gupta et al.[17] They found that 75% of squamous cell carcinoma patients had central lesion. In present study small cell lung cancer presented most commonly as hilar mass (41.7%). Our study is also comparable to various other studies. Rawat et al.[18] also observed that small cell lung cancer presented commonly as central lesion.

Gupta et al.[17] also found that most common location of small cell carcinoma was central (50%). Adenocarcioma most commonly manifests as peripheral mass or a malignant pleural effusion. In present study adenocarcinoma constituted 5.45% of lung cancer, mostly present in upper zone (66.7%) and most commonly associated with pleural effusion. This is comparable with the study conducted by Rawat et al.[18] which observed that adenocarcinoma commonly manifested as peripheral mass or a malignant pleural effusion. This could be explained because of still lower incidence of female smokers in India. Associated pleural effusion was observed in 21.8% cases most of them having squamous cell carcinoma. Squamous cell carcinoma lung was present in 9.1% cases showing evidence of metastasis to liver, bone, adrenal, ipsilateral chest wall and pulmonary metastasis. Computed tomography of the chest and upper abdomen has already been shown to be an important tool in the diagnosis and staging of lung cancer. In our study the computed tomography of chest and abdomen (including adrenals) was done in 79 patients. Majority of patients presented with hilar mass (37.75%). Right lung mass and Collapse/consolidation was seen in 36.25% patients each. Sharma et al[23] reported mass lesion in 30.6% patients followed by collapse consolidation in 13.5% patients. Rawat et al.[18] also reported mass lesion in 46.13% followed by collapse-consolidation 40.89%. Mediastinal lymphadenopathy was detected in 28 patients by CT chest. This is comparable to study conducted by Chhajed et al[24] in which 34% patients present with mediastinal lymphadenopathy. Endobronchial mass lesion was seen in 85% patients in our study followed by vocal cord paralysis in 5% patients. Squamous cell carcinoma was most common(69.38%) histologic subtype in male smokers followed by small cell carcinoma in 24.48% patients. Amongst non-smokers the most common pathological diagnosis was squamous cell carcinoma. This is comparable to the study conducted by Sheikh et al.[25] which observed that among smokers squamous cell carcinoma was the main histological subtype 72.2% followed by small cell

carcinoma 22.9%. There is changing trend of pathological pattern of lung cancer in the West. Women were increasingly diagnosed with Lung cancer having adenocarcinoma as the commonest histological type Kumar et al.[21] In various Indian studies squamous cell carcinoma still being the most common histological subtype.[20,22,24] In the present study also squamous cell carcinoma was observed to be the commonest histological subtype (50%) followed by small cell carcinoma 15%. 3(3.75%) patients present with adenocarcinoma lung. This difference in cell patterns between the Western and Indian studies could be explained by several reasons. In India, prevalence of smoking is less prevalent among women. There may be racial/ethnic differences in disease pattern, which seems to resemble the distribution seen in the West in 1950s and 1960s.[23] The cell type pattern also varies with smoking habits, age and sex. Up to 40 years of age, small cell carcinoma predominates and has a weaker association with smoking. After the age of 40 years, squamous cell type is the commonest type in smokers and adenocarcinoma in non-smokers.[26] The comparison of present study with that of other Indian studies is summarised in Table 6.

CONCLUSION

Thus, our analysis suggests that squamous cell carcinoma still remains the commonest histological subtype. Most of the patients were elderly with smoking as the principal risk factor. Early detection and early treatment to reduce the morbidity and mortality associated with lung cancer in addition to imparting awareness on harmful effects of smoking and how to prevent the disease in general population is the need of this region.

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