Pathology

Neoplastic lesions of the lung – A Prospective Study.

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ABSTRACT Aims : The aims of the present study are to study the neoplastic lesions of lung and to study the incidence of lung cancers with reference to age, gender, lifestyle and occupation.

Materials and Methods: The study is done over a period of 2 years (May 2009 to April 2011) in the Department of Pathology, GGH,Guntur. Total of 32 lobectomy specimens were studied. Formalin fixed, paraffin embedded H & E stained tissue sections were studied. . Immunohistochemistry was done in diagnostically difficult cases.

Results:Majority of lung tumors occurred in the fifth and sixth decade. M:F sex ratio is 4:1. On chest x-ray/CT scan chest, majority of lung tumors presented as mass lesion. Right side of the lung is more commonly affected than the left.Cigarette smoking is the major etiological factor in the causation of lung carcinoma. Among the primary tumors, adenocarcinoma constituted largest group followed by squamous cell carcinoma.

Conclusion: From the present study it is concluded that adenocarcinoma is now the most common lung carcinoma in all race and sex groups. There is a strong association between lung cancer and smoking. Chest radiograph and CT scan aid in the diagnosis and anatomical localisation of lung tumor.

KEYWORDS : Lung, Smoking, Neoplastic, Carcinoma.

INTRODUCTION

Lungs are one of the vital organs in the body and participate in delivering oxygen to and removing the excessive carbon dioxide from the body and enable the smooth functioning of various organs.Lung cancer was a rare disease until the early 1900s but it is now the most common cancer world wide ^[1]. Lung cancer is by far the leading fatal cancer in both men(31%) and women, compared to prostate, colon and rectum^[2]. It began a sharp rise around 1930 in men and in the 1960s in women. Since the early 1950s the disease has become the most common cause of cancer death, rising steadily until 1991 when the mortality rate in men began to decline. In women, the mortality rate has continued to increase. Interestingly, over the years, the incidence by histologic type has significantly changed from squamous cell carcinoma to adenocarcinoma in all race-sex groups^[8]

With more than 1.1 million deaths annually worldwide, lung cancer is the most frequent and one of the most deadly cancer types. In men 85-90% of cases can be attributed to tobacco smoking ^[4]. Some western countries in which the smoking habit took off about 100 yrs ago, tobacco control programme has led to a significant decline in mortality.

The prognosis of lung cancer is still poor, with a 5 yr survival rate of approximately 10% in most countries^[1]. Thus primary prevention by not starting or by stopping smoking remains the most promising approach.

The association between smoking and lung cancer is not solely based on epidemiological studies. Lung tumours of smokers frequently contain a typical though not specific, molecular fingerprint in the form of G:C > T:A. mutations in the TP53 gene which are probably caused by benzo(a)pyrine, one of the many carcinogens in tobacco smoke^[5].

MATERIALS AND METHODS

The prospective study was done over a period of 2 years (May 2009 to April 2011) in the Department of Pathology, GGH, Guntur. Atotal of 32 cases were studied, who presented with a mass lesion on CT scan and X-ray to the cardio thoracic department. Complete clinical details including age, sex, smoking history, family history, duration of complaints and radiological data were collected. The case material included lobectomies. Specimens were fixed in 10% buffered formalin. Tissues were processed by routine paraffin processing. Sections from paraffin blocks were taken and Haematoxylin & Eosin staining was performed. Immunohistochemistry was done in diagnostically difficult cases. Histological typing, grading and tumor extension were studied on tissue sections. The incidence of lung cancers with reference to age, gender, lifestyle and occupation were studied.

Immunohistochemistry was done using the protocol given by the manufacturer. Heat induced antigen retrieval method was followed in our institute. Multistep procedure (sandwich method) was followed using biotinylated universal secondary antibody and a third layer of streptavidin, horse radish peroxidase complex and finally DAB chromogen was used to develop colour at the site of antibody binding.

RESULTS

A prospective histopathologic study of 32 cases of lung lobectomy specimens was done at Guntur Medical College, Guntur from May 2009 to May 2011.

The results of the study are as follows.

Table – 1:Age incidence of various lung tumors.

1	Table – 1.Age meldence of various lung tumors.					
Γ	Age group Neoplasms					
Γ	<10 0					
Γ	11-20	3				
	21-30 1					
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31-40	1
41-50	7
51-60	12
61-70	8
total	32

Table-1 shows that neoplastic lesions are common in the 6 th decade.

Table-2 Gender distribution of various lung tumors

S.no	Lesion	М	F
1	Benign & malignant neoplasms	26(81.25%)	6(18.15%)

Table 3: Laterality of lesion

Side of lesion	No. of cases		
Right side	20		
Left side	12		

Table 4: CT scan findings in patients with carcinoma in the current study.

Mass lesion	26	81.25%
Pleural effusion	2	3.15%
Pleural effusion with mass lesion	4	15%

Table 4 shows that mass lesion in the lung is the most common diagnosis on chest X-ray and CT scan chest.

Table-5 : Incidence of neoplastic lesions in lobectomy specimens

Diagnosis	No of specimens	% of total
Squamous cell carcinoma	11	34.37%
Adenocarcinoma	13	40.62%
Synchronous tumor	1	3.12%
Small cell carcinoma	1	3.12%
Non hodgkin's lymphoma	1	3.12%
PNET	1	3.12%
Secondary deposit from sarcoma	2	6.25%
Synovial sarcoma	1	3.12%
Endobronchial hamartoma	1	3.12%

This table 6 explains the histopathological diagnosis in lung specimens From the table it is clear that adenocarcinoma is more common that is closely followed by squamous cell carcinoma in our study.

Table - 6 Age incidence of lung tumors

Age	AdenoCa	Sq.	SCC	ES /	SS	Thymom	NHL	met	hamartom
range		CC		PNET		а		S	а
10-20	0	0	-	1	-	-		1	0
21-30	0	0	-	-	-	-	-	-	0
31-40	0	0	-	-	-	-	-	-	0
41-50	5	0	-	-	-	-	1	-	1
51-60	6	7	1	-	1	1	-	1	-
61-70	2	3	-	-	-	-	-	-	-
> 70	0	1	-	-	-	-	-	-	-
Total	13	11	1	1	1	1	1	2	1

This table 6 clearly depicts that lung carcinomas are more common in the sixth decade.

Table 7: Staging of lung tumors in radical specimens

Stage IA	1
Stage IB	8
Stage IIA	0
Stage IIB	6
Stage IIIA	0
Stage IIIB	0
Stage IV	0

Out of 29 lung malignancies, 2 cases are metastases from sarcomas. For Lymphoma, Synovial sarcoma and Ewing's sarcoma TNM staging is not applied. TNM staging is also not applied for small cell carcinoma. In remaining 15 cases, 8 cases are in stage IB, 6 cases are in stage IIB and 1 case in stage IA

DISCUSSION

The present study is undertaken to study the spectrum of neoplastic lesions of lung and to correlate the clinical, radiological and histopathological features of various lung tumors.

Paraffin embedded and H & E stained tissue sections are studied and discussed in the light of other research findings in the literature.

Although the lungs are frequently the site of metastases from cancers in extrathoracic organs, primary lung cancer is also a common disease. Bronchial epithelium is the site of origin for 95% of primary lung tumors (carcinomas); the remaining 5% are a miscellaneous group that includes bronchial carcinoids, mesenchymal malignancies (e.g., fibrosarcomas, synovial sarcoma), lymphomas, and a few benign lesions ^[5].

The present study is undertaken to study incidence of different types of lung tumors in and around Guntur.

Eric B Haura et al ^[6] reported that the majority of the cases occured in the fifth, sixth and seventh decades with the peak incidence in sixth decade. The age distribution of various malignant lesions in the present study reflected a similar picture (Table -1)

Eric B Haura, Susan A et al ^[5] recorded a ratio of 5.2:1 and Malhotra et al reported the ratio of male to female ratio as 7.7:1 with a male preponderance. In the present study, sex ratio is 4:1 and is similar to study done by MC. Diffie et al.

Most of the patients presented with cough and shortness of breath. Few patients presented with hemoptysis.

Majority of the lung cancer cases (81.25%) on CT scan presented with mass lesion.

The right lung is more commonly affected than the left. In the right lung, the upper lobe is more commonly involved (68.96%) than middle lobe (24.13%) and lower lobe (17.24%).

Cigarette smoking is one of the causative factor in most cases of lung cancer. Lung tumors of smokers frequently contain a typical though not specific, molecular fingerprint in the form of G:C > T:A. Mutations in the TP53 gene which are probably caused by benzo(a)pyrine, one of the many carcinogens in tobacco smoke^[5]. Not only the neoplastic lesions, non- neoplastic lesions like obstructive and restrictive pulmonary diseases and occupational lung diseases cause significant morbidity

Adenocarcinoma is the most frequent non small cell lung cancer, representing 35-40% of all lung cancers $^{\rm [6]}$. In the present study also, adenocarcinoma is the commonest lung cancer, representing 62% of all lung cancers.

Adenocarcinomas comprise approximately half of all lung carcinomas in females, however, in absolute numbers they are more common in males than in females ^[4]It develops more frequently than any other histologic type of lung cancer in individuals who have never smoked ^[7]

In this study, a denocarcinomas comprise about 40.62% of total malignancies in females.

In contrast to adenocarcinoma, squamous cell carcinoma is found in the central part of the lung $^{[4]}$. In this study, squamous cell carcinoma cases are accounting for 34.67% of all lung cancers. This is similar to a study by Winston W tan et al.

The incidence of primary synchronous lung tumors is around 1.2-5.1% of all non small cell lung cancers and 1.9-9% of those non small cell cancer patients undergoing curative lung resection⁽⁸⁾.

Synchronous tumors include tumors of different histologic types or two tumors of the same histologic type in separate lobes with no evidence of extrathoracic disease.

One case of synchronous lung tumor is reported in our study in a 60 yr old male patient, Histologically, sections from upper lobe mass showed moderately differentiated squamous cell carcinoma and sections from middle lobe mass showed well differentiated adenocarcinoma with focal bronchioloalveolar patterns.

Histopathology of small cell carcinoma is characteristically showed tumor cells arranged in nesting pattern, trabecular pattern. Cells are two times larger than lymphocytes with granular, salt-pepper chromatin, high mitotic activity and characteristic nuclear moulding with vast areas of necrosis.

Small cell carcinoma should be staged as limited versus extensive disease rather than using the TNM system because of the tendency for widespread dissemination at presentation ^[9].Small cell lung cancers have invariably spread by the time they are first detected, even if the primary tumor appears small and localised. Thus surgical resection is not a viable treatment.

Primary pulmonary lymphoma is defined as a lymphoma affecting one or both lungs, without evidence of extra pulmonary involvement or bone marrow disease on diagnosis or during the subsequent 3months^[10]. Primary pulmonary lymphoma represent 0.4% of all lymphomas and 15-30% of rare pulmonary tumors.^[11]

Primary pulmonary synovial sarcomas are rare, constituting less than 0.5% of all pulmonary malignancies ⁽⁶⁾ .Pulmonary Synovial Sarcoma usually presents in young to middle age adults and shows no gender predilection. In this study one case of primary synovial sarcoma is reported which showed positivity of tumor cells to EMA, CK, Vimentin on immunohistochemistry.

Although peripheral primitive neuroectodermal tumors are exceedingly rare, the annual incidence of tumors from the larger Ewing family of tumors (EFT's) from birth to age 20 years is 2.9 per million population ^[12]. One case of Ewing sarcoma / Peripheral neuroectodermal tumor is reported in our study in a 20 year old male patient, which is similar to world literature.

Peripheral primitive neuroectodermal tumors typically co-express CD99 (glycoprotein MIC2) and vimentin $^{\scriptscriptstyle [13]}$

Present case also showed positivity for CD99 and vimentin and negative for EMA, pan cytokeratin, CD45, desmin.

Lungs are frequently the site of metastases from cancers in extra thoracic organs. Most common sources of metastatic tumours to lung, in relative order of frequency are breast, colon, stomach, pancreas, kidney, melanoma, prostate, liver, thyroid, adrenal, male genital and female genital tract^[13]

Two cases of metastatic lesions are reported in our study, among the two metastatic lesions – one case of osteosarcoma deposit in lung occurred in a 18 yrs old female patient with a history of amputation of right leg for osteosarcoma 2 yrs prior to this surgery. Histopathology showed lace like osteoid surrounded by pleomorphic spindle cells.

One case of pleomorphic sarcoma deposit in lung occurred in 55 years old male patient with past history of amputation of right upper limb for pleomorphic malignant fibrous histiocytoma. Histopathology showed pleomorphic spindle shaped tumor cells in storiform patterns and in intersecting fascicles. Tumor cells show high mitotic activity, hyperchromatic nuclei, large, bizarre tumor giant cells.

According to world literature, the incidence of pulmonary hamartoma is 0.25% with a 2-4 fold male predominance and peak incidence in the 6th decade^[14]

In the present study, one case of pulmonary intrabronchial (endobronchial) hamartoma is reported. Gross presentation is a gray white mass situated in the proximal bronchus. Histologically, sections showed predominantly adipose tissue with lobulated masses of cartilage with small clefts of respiratory epithelium.

Conclusions:

Adenocarcinoma is now the most common lung carcinoma in all race and sex groups. There is a strong association between lung cancer and smoking. Chest radiograph and CT scan aid in the diagnosis and anatomical localisation of lung tumor. Immuno histochemistry is very much helpful in diagnosing difficult cases.

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Figure 1: Gross picture of squamous cell carcinoma



Figure 2: Squamous cell carcinoma x100,H&E



Figure 3: Adenocarcinoma-x100, H&E



Figure 4: Small cell carcinoma x100-H&E.



Figure 5: x-ray chest showing mass lesion



Figure 6:CT scan showing hilar mass



Figure 7:ES/PNET -x40, H&E



Figure 8: CD 99membrane +ve in ES/PNET



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Figure 9:synovial sarcoma, x40, H&E



Figure 10:EMA +ve in spindle cells.

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