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Study of Clinicopathological, Autopsy and Histopathological Correlation of Primary and Metastatic Lung Malignancies

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ABSTRACT

Lung cancer is currently the most frequently diagnosed major cancer in the world and the most common cause of cancer mortality worldwide. Present study was aimed to study clinicopathological, autopsy and histopathological correlation of primary and metastatic lung malignancies at a tertiary hospital. Present study was single-center, cross sectional, observational study, conducted in patients of Age >20 years, either gender, known or suspected cases of malignancies involving lungs and incidentally found cases at autopsy. Out of 51 cases, 24 (47.05%) were primary tumours of lung. And 27 (52.9%) were metastatic tumours. Mean age of presentation in primary lung cancer cases is 53.4 yrs. 35 were males (68.6 %) and 16 were females (31.3 %). Along with 10 cases (41.67%) with history of smoking, 9 cases (37.5%) were observed with no addiction, followed by 3 cases (12.5%) of chronic alcoholism and 2 cases (8.33%) of chronic tobacco chewer. Histopathologically, adenocarcinoma was found to be the most common type of primary lung cancer (41.67%) in our study followed by squamous cell carcinoma (24%). Small cell carcinoma was found in 16.67% cases, while single case of Adenosquamous and Large cell carcinoma comprising 4.16% was observed. Out of 24 cases in 16 cases there was evidence of metastasis, that to most commonly to Hilar LN in 8 cases i.e. 33.3% followed by Liver (7 cases i.e. 29.16%) and Adrenals (4 cases i.e. 16.6%). Majority of patients i.e. n=22 is died due to Respiratory failure followed by Cachexia (n=13) and Disseminated malignancy (n=9). From the present study we conclude that secondary Lung malignancies outnumber the primary. Majority cases of lung cancer were misdiagnosed clinically as TB. Our study also reflects the global trend of rise in adenocarcinoma histology.

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Key Words
Clinicopathological, autopsy, histopathological, metastatis, lung malignancies

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INTRODUCTION

Lung cancer is currently the most frequently diagnosed major cancer in the world and the most common cause of cancer mortality worldwide. This is largely due to the carcinogenic effects of cigarette smoke[1]. The current male: female ratio is 1.5: 1. More than 90% of the patients are over 40 years of age at the time of diagnosis, but cases have also been reported in young adults and adolescents[2].

However, approximately 10-15% of cases of lung carcinomas occur in never-smokers. Among them, three-fourths are women and a high proportion of cases show an adenocarcinoma histology. Adenocarcinoma occurring in never-smoker women appears to be more prevalent in Asian population[3]. Most lung cancers are of considerable size when first detected and about 60% are incurable as a result of extensive local spread and/or distant metastases. Symptoms and signs develop relatively late in the course of the disease, are usually related to partial or complete bronchial obstruction and may lead to confusion with a primary inflammatory process[4].

The relative frequencies of the various microscopic types of lung carcinoma have changed over the years. Squamous cell carcinoma used to be the more common type, but at present there is a majority of adenocarcinomas[2]. Present study was aimed to study clinicopathological, autopsy and histopathological correlation of primary and metastatic lung malignancies at a tertiary hospital.

MATERIAL AND METHODS

Present study was single-center, cross sectional, observational study, conducted in department of pathology, at LTMG Hospital, Sion Mumbai, India. Autopsy cases with final cause of death as Lung malignancy including metastasis performed during period of January 2001 up to September 2013 were included in study. Study approval was obtained from institutional ethical committee.

Inclusion Criteria:

- Patients of Age >20 years, either gender, known or suspected cases of malignancies involving lungs and incidentally found cases at autopsy.

Exclusion Criteria:

- All medicolegal autopsies having history of fall, trauma, poisoning, burns etc.

Gross description of both the lungs studied on fresh and after fixation in formalin for adequate duration. After preservation, at least 4 sections from tumour and 2 sections from uninvolved lung parenchyma taken. Representative sections from other organs also taken. Sections studied by using H and E stain and special stains wherever indicated. Case history retrieved by going through indoor case papers. Retrospective autopsy cases were studied by using autopsy notes, the blocks and slides retrieved and rescreened for any additional pathology. Parameters to be studied were clinical presentation, chest X-ray findings, gross description of organs, microscopic findings and diagnosis.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Statistical analysis was done using descriptive statistics.

RESULTS AND DISCUSSIONS

A study of 51 autopsy cases of lung cancer was undertaken to study the clinicopathological correlation and histopathological presentation. Out of 51 cases, 24 (47.05%) were primary tumours of lung. And 27 (52.9%) were metastatic tumours.

Mean age of presentation in primary lung cancer cases is 53.4 yrs. Out of 24 cases of primary lung cancer, majority of cases i.e. 14 (58.33%) belongs to age group 41-60yrs followed by 61-80yrs age group contributing 25%. 4 cases i.e. 16.67% falls into 21-40 yrs. age group. Similarly, out of 27 cases of metastatic lung tumours, majority i.e. 12 cases (44.4%) belong to age group 41-60 yrs. followed by 21-40yrs age group contributing 9 (33.3%) cases.

Out of total 51 cases, 35 were males contributing to 68.6% and 16 were females comprising of 31.3%. Amongst 24 primary lung cancer cases, 62.5% i.e. 15 were males and 9 cases (37.5%) were females. The Male: Female ratio of primary lung cancer was found to be 1.6: 1.

Most common clinical presentation observed to be Breathlessness in 16 out of 24 primary lung cancer cases i.e. 66.6% followed by Cough in 12 (50%) cases. Fever is seen in 12 (50%) cases and Weight loss in 7 (29.1%) cases. 3 Cases of Hemoptysis, 2 cases of Chest pain and 2 cases of Pain in abdomen were observed.

Out of 24 primary lung cancer cases diagnosed at autopsy only 11 cases were suspected as malignancy with other differential diagnosis clinically.13 cases were not suspected as malignancy antemortem. Out of these 13 undiagnosed cases 7 cases were diagnosed as TB.

Along with 10 cases (41.67%) with history of smoking, 9 cases (37.5%) were observed with no addiction, followed by 3 cases (12.5%) of chronic alcoholism and 2 cases (8.33%) of chronic tobacco chewer. 5 cases (20.8%) with combination of chronic smoking and occasional alcohol intake were noted.

Histopathologically, adenocarcinoma was found to be the most common type of primary lung cancer (41.67%) in our study followed by squamous cell

carcinoma (24%). Small cell carcinoma was found in 16.67% cases, while single case of Adenosquamous and Large cell carcinoma comprising 4.16% was observed. A single case of Signet ring cell adenocarcinoma was noted in our study. A25 year old female presented with breathlessness, low grade fever and cough with expectoration of 3 months duration associated with weight loss and anorexia. She was clinically diagnosed as pulmonary Koch's. No radiological investigations were done. No other positive finding on general and systemic examination were noted.

On autopsy examination, both lungs were boggy voluminous with firm whitish patchy areas of consolidation on cut surface. All other organs were unremarkable. On histological study, section shows solid sheets of round to polygonal cells with abundant intracytoplasmic mucin which was confirmed by Mucicarmin stain. As all other organs on gross and histology were unremarkable, this case was labelled as Primary signet ring cell carcinoma of lungs.

In the present study most, common macroscopic presentation was Single mass lesion seen in 10 cases out of 24 cases i.e. 41.67% cases. Single mass lesions were central in location in 8 cases, with 1 peripheral and 1 lobar in location. Second common presentation was Bronchopneumonia like comprising 16.67% followed by Multiple nodular, Cavitatory presentation and pulmonary edema each comprising 12.5%.

Out of 24 cases of primary lung malignancy 20 cases have Chest X-ray records. Most common chest X-ray

Table 1: General characteristics

Characteristics	Primary (n=24)	Metastasis (n=27)
Age groups (in years)		
21-40	4 (16.67%)	9 (33.3%)
41-60	14 (58.33%)	12 (44.4%)
61-80	6 (25%)	6 (22.2%)
Gender		
Female	9 (37.5%)	16 (31.3%)
Male	15(62.5%)	35 (68.6%)
Presenting symptom in primary		
Cough	12 (50 %)	
Breathlessness	16 (66.67 %)	
Weight Loss	7 (29.1 %)	
Fever	12 (50 %)	
Chest pain	2 (8.3 %)	
Hemoptysis	3 (12.5 %)	
Pain in abdomen	2 (8.3 %)	
Primary lung cancer (n=24)		
Unsuspected malignancy	13 (54.16 %)	
Suspected malignancy	11 (45.83 %)	

Table 2: Distribution of cases according to Addiction

Type of addiction	Frequency	Percentage
Chronic smoker	10	41.67%
Chronic Tobacco chewer	2	8.33%
Chronic Alcoholics	3	12.5%
Chronic smoker and tobacco chewer and occasional alcohol intake	5	20.8%
No addiction	9	37.5%

Table 3: Distribution of cases according to Histological type of cancer

	Smoker	Non-smoker	Total
Squamous cell carcinoma	6 (25%)	2 (8.3%)	8 (33.3%)
Adenocarcinoma	3 (12.5%)	7 (29.16%)	10 41.67%)
Small cell carcinoma	1 (4.16%)	3 (12.5%)	4 (16.67%)
Adenosquamous carcinoma	-	1 (4.16%)	1 (4.16%)
Large cell carcinoma	-	1 (4.16%)	1 (4.16%)
Total	10 (41.67%)	14 (58.3%)	(100%)

Table 4: Macroscopic presentation of primary lung cancer [n=24]

Presentation	Frequency	Percentage
Single mass lesion	10	41.67%
Bronchopneumonia like	4	16.67%
Multiple Nodules	3	12.5%
Cavity	3	12.5%
Scar	1	4.16%
Pulmonary edema	3	12.5%

Table 5: Distribution of primary lung cancer cases according to Chest X- ray findings [n=20]

Chest X-ray findings	Number of cases	Percentage
Mass lesion	10	41.67
Pleural effusion	4	16.67
Consolidation	4	16.67
Massive infiltration? Bronchogenic carcinoma	1	4.16
Tuberculous infiltrates	1	4.16

Table 6: Metastasis of primary lung cancer to other organs [n=24]

	Frequency	Percentage
Metastasis present	16	66.67
Hilar LN	8	33.33
Liver	7	29.16
Adrenals	4	16.67
Kidneys	3	12.5
Diaphragm	1	4.16
Paratracheal LN	1	4.16
Left supraclavicular LN	1	4.16
NO METS	8	33.33

Table 7: Distribution of metastatic lung cancer cases according to their site of primary [n=27]

Presentation	Frequency
Pancreas	3 (11.53%)
Liver	2 (7.69%)
Uterus- Choriocarcinoma	2 (7.69%)
Lower limb- Liposarcoma	1 (3.84%)
Ovary	1 (3.84%)
Testis	1 (3.84%)
Thyroid	1 (3.84%)
Breast	1 (3.84%)
Foot	1 (3.84%)
Stomach	1 (3.84%)
Small intestine	1 (3.84%)
Colon	2 (7.69%)
Oral cavity	1 (3.84%)
Anorectal	1 (3.84%)
Gall bladder	1 (3.84%)
RCC	1 (3.84%)
Unknown	5 (19.23%)

Table 8: Distribution of secondary lung cancer cases according to macroscopic presentation.

Presentation	Frequency	Percent
Multiple nodules scattered throughout all lobes	14	51.8%
No gross abnormality	6	22.2%
Consolidation	4	14.8%
Single nodule	2	7.4%
Pleural nodules	1	3.7%

Table 9: Distribution of cases according to cause of death in all cases.

Cause of death	Primary lung cancer	Secondary lung
cancer		
Respiratory failure	14	8
Cachexia 6	7	
Cardiorespiratory Failure	2	-
Disseminated malignancy	2	7
Hepatic failure	-	2
Multiorgan failure	-	1
Acute renal failure	-	1
Septicemia	-	1
TOTAL	24	27

finding was mass lesion (n=10) followed by Pleural effusion and Consolidation (n=4)

Out of 24 cases in 16 cases there was evidence of metastasis, that to most commonly to Hilar LN in 8 cases i.e. 33.3% followed by Liver (7 cases i.e. 29.16%) and Adrenals (4 cases i.e. 16.6%).

Out of total 51 cases of lung cancers 27 were metastatic i.e. secondary tumours which comprises 52.9%.

Most common pattern of metastatic lung tumours observed is multiple nodules scattered throughout all lobes more being at periphery, which comprises of 15 cases (55.5 %). Second common pattern observed was microscopic foci of tumour cells without any evidence of gross findings which is present in 6 cases i.e. 22.2%, followed by this was Pneumonic consolidation (4 cases,14.8%) and single nodular pattern (2 cases,7.4%). Single case of pleural involvement is seen.

Majority of patients i.e. n=22 is died due to Respiratory failure followed by Cachexia (n=13) and Disseminated malignancy (n=9).

Currently, a lung cancer in India is one of the most lethal cancers, accountable as the fourth largest cause of cancer mortality. Among males, it is a largest cause of mortality accounting for 13% of all cancer deaths[5] and its incidence is rising among women.

The age range in present study is 21-80 yrs. with mean age of 53.4yrs and most common age group involved is 41-60 yrs. comprising 58.3 % cases. Mean age of the present study i.e. 53.4 yrs. correlate with the Jindal and Behera study[6] (54yrs), Krishnamurthy[7] (56 yrs.) and Noronha[5] studies. Maximum cases found in 41-60 yrs. age group which is also comparable to the Krishnamurthy[7] (40-60 yrs.) and Noronha[5] (40-60 yrs.).

In the Present study, out of 24 primary lung cancer cases, 14 were males i.e. 62.5% and 10 were females i.e. 37.5%, with M:F ratio 1.6 :1. This ratio is low as compared to various other studies. In Noronha[5] study Out of 489 patients, there were 380 (77.7%) males and 109 (23.3%) females i.e. a male: female ratio of approximately 3.5:1. In Mahesh[8] study, there were 128 males and 42 females, with male: female ratio of 3:1. also In Krishnamurthy[7] study, the male: female ratio was approximately 3.5:1; there were 200 (77.5%) males and 58 (22.5%) females.

With regard to smoking status, none of the females were smokers while 66.7%males were smokers in present study, these findings correlate with Krishnamurthy[7](91% females non-smokers) and Noronha[5] (88.1% females nonsmokers). More than half of the total cases are non-smokers in Mahesh[8] study (54.1%) and Noronha *et al.* study[5] (52.1%) which correlates with the present study comprising 58.3% non-smokers.

Over the past four decades, there has been a shift in the pathologic distribution of non-small cell lung cancer i.e. NSCLC. Prior to the 1970s, squamous-cell carcinoma was the most common histological type of NSCLC, however, since about 1975., there has been a dramatic increase in the incidence of adenocarcinoma, making it the predominant histological subtype of NSCLC[9]. Thus far, not much information was available as to the distribution of the histological subtypes in India. A review article from 2004 stated that squamous-cell carcinoma was still the predominant histological subtype of NSCLC in India[10]. According to Jindal and Behera study6, squamous cell carcinoma is found in 34.3%, anaplastic in 27.6% adenocarcinoma in 25.9% and unclassified in 12.2%. While in many Western countries adenocarcinoma has become the commonest histological type of lung cancer in India it is still squamous cell carcinoma in both males and females.

Results from our study suggest that a pathologic shift may have occurred in India as well. In the Present study, most common histological type is Adenocarcinoma (41.7%) followed by Squamous cell carcinoma (33.3%), Small cell carcinoma (16.7%). These findings correlate with the Mahesh[8] study, Krishnamurthy[7] study and Noronha[5] study which also shows Adenocarcinoma as most common histological type. In Mahesh[8] study, most common histological type of lung cancer was Adenocarcinoma (32.9%) followed by Squamous cell carcinoma (15.9%), Small cell carcinoma (11.17%) and large cell carcinoma (2.9%) And remaining 37% cases were unclassified histologically. In Krishnamurthy[7] study, non-small-cell lung cancer (NSCLC) was the predominant histology in 224 patients (86.8%)., Within NSCLC, the most common histology was adenocarcinoma (42.6%) followed by squamous cell carcinoma, (15.6%). In Noronha[5] study, Small-cell carcinoma was diagnosed in 8% of patients, while 92% of the patients had NSCLC. Within NSCLC, the most common histology was adenocarcinoma (43.8%) followed by squamous-cell carcinoma (26.2%),

Traditionally, squamous-cell carcinoma of the lung was thought to be smoking-related, rather than adenocarcinoma. The increase in the incidence of adenocarcinoma was thought to be mainly attributable to a change in smoking pattern and an increased preference for filter cigarettes that have low tar, but high nitrate content[10]. Earlier studies reported that the increased incidence of adenocarcinoma was confined to smokers[11,12]. In contrast, we found a statistically higher occurrence of adenocarcinoma in non-smokers as compared to smokers. This is supported by other studies in the literature[10,13,14,15,16].

A single case of signet ring cell adenocarcinoma of lung

was noted in the present study. This is very rare variant of adenocarcinoma[17,18,19]. Fibrotic scars are frequently found in proximity to lung cancer at the time of cancer diagnosis. However, the nature of the relationship between pulmonary scarring and lung cancer remains uncertain. According to one study, the relationship between pulmonary scarring and lung cancer was specific to the same lung and extended over time. These findings were consistent with the hypothesis that localized inflammatory processes associated with scarring promote the subsequent development of lung cancer.[73] Some believe that the atypical epithelial proliferation and in a further step, malignancy, are the results of an abortive effort of the damaged epithelium to regenerate[20].

In the present study most, common radiologic presentation was Single mass lesion seen in 10 cases out of 24 cases i.e. 41.67% cases. Single mass lesions were central in location in 8 cases, with 1 peripheral and 1 lobar in location. This is followed by Pleural effusion (16.67%) and Consolidation (16.67%). All these findings correlate with the both above mentioned studies. In Jindal and Behera study[6], the commonest presentation was mass lesion with or without collapse in 68%, 25% had pleural effusion and 16.7% superior vena caval compression syndrome.

Lung cancer is one of the most insidious and aggressive neoplasms in the whole realm of oncology. In the usual case, it is discovered in patients in their fifties whose symptoms are of several months' duration. In present study 7 out of 24 lung cases (29.16%) were diagnosed as TB and treated accordingly. Similar findings were observed in various other studies. In Noronha[5] study., sixty-nine patients (14.1%) were incorrectly diagnosed and treated with anti-tuberculosis treatment, which delayed the diagnosis of lung cancer by four months.

The symptoms such as cough, dyspnea, chest pain, hemoptysis and weight loss are common to both tuberculosis and lung cancer irrespective of their smoking status. It is not uncommon to find a lung cancer patient in India being treated for tuberculosis initially[21,22,23]. The delays in diagnosis in developing countries like India can be attributed to many factors-patients' ignorance in reporting to general practitioners, misinterpretation of chest radiograph findings and starting anti-tuberculosis therapy for suspicious opacities on the chest radiograph without proper evaluation[22,23]. The association of dual pathology is also known[5].

In the present study, out of 24 cases in 16 cases there was evidence of metastasis i.e. 66.7%, that to most commonly to Hilar LN in 8 cases i.e. 33.3% followed by Liver (7 cases i.e. 29.16%) and Adrenals (4 cases i.e. 16.6%). The percentage of cases showing metastasis, 66.7% is comparable with the Jindal and Behera study[5] with 51.8% cases of metastasis and distribution of local (33.3%) and distant (66.7%) metastasis is comparable with the Mahesh[8] study (local-34.1%, distant-65.9%).

CONCLUSION

From the present study we conclude that secondary Lung malignancies outnumber the primary. Majority cases of lung cancer were misdiagnosed clinically as TB. Our study also reflects the global trend of rise in adenocarcinoma histology. However, these observations need to be substantiated in similar studies of larger magnitude, preferably population-based.

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