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MYRIAD CLINICAL PRESENTATIONS OF LUNG CANCER: A SINGLE CENTRE CROSS-SECTIONAL STUDY AT A TERTIARY CARE CENTRE IN WEST INDIA

Oncology

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ABSTRACT

BACKGROUND: Lung cancer is the leading cause of cancer death globally and is now considered as the commonest fatal malignancy in the developed world. India contributes to 20% of all deaths due to lung cancer in the world.

METHODS: To study the clinical and paraneoplastic presentations of lung cancer, we carried out a single centre, cross sectional observational study on a cohort of 100 patients of freshly detected Lung cancer.

RESULTS: Mean age of the subjects was 56.36 years and 30% of the cases were above 60 years of age. Majority (63%) of them were males and smokers (59%). Most common presenting symptoms were cough (22.21%), chest pain (16.13%), fever (14.37%), dyspnoea (11%) and hemoptysis (5.22%). Paraneoplastic syndromes comprised of anemia and leucopenia (20%) cases followed CNS manifestation (in 8%) cases. No association was observed between type of lung carcinoma and paraneoplastic syndrome.

CONCLUSION: Our study confirms the high prevalence of lung cancer in male smokers with predominantly respiratory complaints. Paraneoplastic syndromes are not a rare entity in such patients and a high level of clinical suspicion is required for early detection of such cases.

KEYWORDS

Lung Cancer, Anemia, Paraneoplastic, Smokers

1. INTRODUCTION

Lung cancer is the leading cause of cancer death in developed countries and is now considered as the commonest fatal malignancy in the developed world. [2] The same scenario can now be seen in developing countries where it is rising at alarming rates. [3] In India, lung cancer was initially thought to be extremely rare, [4] but now 1 million of the current 5 million deaths in world, and 2.41 million in developing countries is contributed by India [5,6] and, in 2020, this figure is projected at 1.5 million! [4, 7] In Indian, patients with lung cancer, history of active tobacco smoking was found in 87% of males and 85% of females. History of passive tobacco exposure is found in 3%. So, 90% of all cases result from tobacco exposure.[8] The major risk factor for developing lung cancer is tobacco use and this disease is often viewed solely as a smoker's disease. [9] Two major types of lung cancer are non small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). Adenocarcinoma, squamous cell carcinoma and large cell carcinoma are classified under non small cell carcinoma of lung. [10] In Indians, however, SCLC is predominant over NSCLC. [11] Smoking is responsible for upwards of 80% of all lung cancers worldwide. [12] Other reasons are combination of genetic factors, radon gas, asbestos, pesticides [13] and air pollution including passive and static smoking. Clinical presentations of lung cancer patients in India [10,14] are cough with expectoration (40.0-94.3%), chest pain (16.0-66.7%), loss of weight (11.4-90.0%), breathlessness (24.0-59.0%), weakness (4.0-90.0%), haemoptysis (8.0-69.2%), fever (19.6-68.6%), anorexia (20.5-90.0%), hoarseness of voice (9.0-33.0%), nausea and vomiting (6.0-25.0%), puffiness of face (2.9-19.8%), dysphagia (2.9-20.8%). These symptoms doesn't appears until the cancer is advanced, that's why diagnosis of lung cancer in our country is generally delayed. Also, incidence rate of distant metastasis is very high in lung cancer

In our country, there is a lack of public awareness about common signs and symptoms of lung cancer. So, it is very important to note that the early symptoms of lung cancer may be very subtle or vague. Instead of identifying disabling hoarseness, someone may simply notice that he is clearing his throat more frequently than expected. Instead of having only shortness of breath, a person may simply think that he is out of shape or has gained few pounds when he becomes winded walking up a flight of stairs. So, initial presentation of lung cancer can be variable and different in some patients. It is very important to collect a data regarding most common and early presentation of lung cancer.

In present study, we thus aimed to evaluate the clinical and paraneoplastic presentations of lung cancer in tertiary level hospital.

2. PATIENTS AND METHODS

2.1 STUDY DESIGN

We carried out a cross-sectional observational study on 100 consecutive adult patients with Lung cancer admitted to an Oncology unit of a tertiary care center in western India during the 2017-2019 period.

2.2 POPULATION

We enrolled all patients whose demographic, clinical and anamnestic data were available. Laboratory results were extracted from the laboratory database. All consenting adult patients more than 18 years of age with a fresh histopathological diagnosis of Lung cancer were included in the study. All patients below 18 years of age, patients with metastases to lung and those not willing to give written consent were excluded.

2.3 METHODOLOGY

A detailed medical history of the patients regarding their clinical symptoms, past medical or surgical history, occupational history was taken. The smoking history included the current status, the mode of smoking, and any other mode of tobacco intake. ECOG (Eastern Co-operative Oncology Group)/ WHO (World Health Organisation) performance status was also evaluated.

Histopathological reports were taken as basis for classifying type of tumor and stage of tumor.

2.5 STATISTICAL ANALYSIS

The quantitative data was represented as their mean ± SD. Categorical and nominal data was expressed in frequency and percentage and analyzed by using chi-square test. The significance threshold of p value will be set at <0.05. All analysis were carried out by using SPSS software version 21.

3. RESULTS

A total of 100 consecutive cases attending our Oncology OPD during the study period were included in the study. The mean age of the patients was 56.36 years and 30% of the cases were over 60 years of age. Majority (63%) of the patients were males. Most common associated co-morbidity was type 2 diabetes (21.77%) ,hypertension (16.93%), COPD (11.29%) and old tuberculosis (8.06%) as depicted in Table 1. Of all ,70 % cases were smokers (both active and passive).

Table 1. Distribution of study subjects as per co-morbidities

Co-morbidity	N	%
Diabetes mellitus	27	21.770%

Hypertension		21	16.930%
Chronic Obstructive Pulmonary Disease		14	11.29%
Tuberculosis		10	8.06%
Other	**Stroke**	09	7.25%
	Seizure	06	4.83%
	Dyslipidemia	5	4.03%
	Coronary artery disease	4	3.22%
	Chronic liver disease	2	1.61%
	Gout	2	1.61%
	Schizophrenia	1	0.806%
No comorbidities	23	18.54%	

Patients in this study group were having predominant respiratory symptoms (39%) which comprised of cough, dyspnoea, wheeze, hemoptysis and chest pain (Table 2).

Table 2: Distribution of study subjects as per presenting com p laints

Symptoms		**N**	**%**
Cough	**<3 weeks**	8	5.22%
	3-8 weeks	9	5.88%
	> 8 weeks	17	11.11%
Dyspnoea	**< 1 month**	8	5.22%
	≥ 1 month	9	5.88%
Chest Pain		25	16.33%
Hemoptysis		8	5.22%
Wheeze		3	1.96%
Fever		22	14.37%
Head ache		10	6.53%
Back ache and/or bone pain		9	5.88%
Anorexia		8	5.22%
Weight Loss		7	4.57%
Easy Fatigability		7	4.57%
Hoarseness of voice		2	1.31%
Seizure		1	0.65%
Total		153	100%

Non-specific symptoms of other system (focal weakness, fever, anorexia, hoarseness of voice, weight loss, etc) were observed in 55% cases. Significant amount of cases were cachexic (6%) and underweight (3%) while 5% were overweight by BMI. (Note- case with Cushing's syndrome as a paraneoplastic manifestation is included in overweight category)

On general examination, lymphadenopathy (axillary and cervical group of lymph nodes) and clubbing was observed in 16% and 19% cases while pallor and cachexia (BMI- < 16Kg/m2) was seen in 12% cases and 6% cases each respectively.

A wide range of paraneoplastic syndromes were seen in the present study. Hematological manifestations like anemia, leukopenia and thrombocytopenia were seen in 20% cases while CNS abnormalities (like cerebellar ataxia, transverse myelitis, peripheral neuropathy, seizure, lambert eatons myasthenic syndrome etc.) were seen in 8% cases.

Table 3. Distribution of study subjects as per type of parane opl astic syndrome

Paraneoplastic Syndrome	**N**	**%**
Hematological Manifestations	20	20.0%
CNS Manifestations (Encephalopathy, Cerebellar ataxia, Opsoclonus, transverse myelitis, Peripheral neuropathy, etc)	8	8.0%
Hypercalcemia of malignancy	6	6.0%
SIADH	6	6.0%
Dermatomyositis/ Polymyositis	2	2.0%
Horner Syndrome	2	2.0%
Cushing's syndrome	1	2.0%

Other common paraneoplastic syndromes were SIADH and hyperca lcemia in 6% and 4% cases respectively. Dermatomyositis/ polym yos itis and Horner's syndrome was seen in 2% cases each (Table 3)

Most common type of lung malignancy was adenocarcinoma (53%) followed by small cell carcinoma (22%) and squamous cell carcinoma (19%).

A significant association was observed between squamous cell carcinoma with male gender and history of smoking. Positive x-ray findings were seen in all the 6 cases of large cell carcinoma (pleural effusion in 4 and consolidation in 2 cases). No strong association was observed between type of lung carcinoma and paraneoplastic syndrome as shown in Table 4. Though maximum cases (23) were seen with Adenocarcinoma.

Table 4. Associations of study variables with type of lung carc inoma

Diagnosis	**NO.**	**Males**	**Smokers**	**Positive X-ray finding**	**Para-neoplastic Syndrome**
Adenocarcinoma	53	25 (47.2%)	32 (60.4%)	29 (50.87%)	23 (43.39%)
Squamous cell carcinoma	19	17 (89.5%)	18 (94.7%)	9 (47.36%)	10 (52.6%)
Large cell carcinoma	6	3 (50.0%)	4 (66.7%)	6 (100.0%)	3 (50.0%)
Small cell carcinoma	22	18 (81.8%)	19 (86.4%)	13 (59.09%)	9 (40.9%)

DISCUSSION

Lung cancer is the most common cancer diagnosed worldwide. It is also the leading contributor to cancer-related mortality, resulting in around 1.38 million cancer deaths per year worldwide.

Till date, the discrepancies between patients with symptomatic lung cancer and asymptomatic lung cancer have been observed by several studies, most studies placed asymptomatic lung cancer patients detected by screening or incidentally as the research subjects while treated symptomatic lung cancer patients with initial respiratory symptoms as the controls. Few studies have concentrated on describing the clinico-pathological characteristics of lung cancer patients visiting due to present initial respiratory symptoms.

Present study was done to study the initial clinical presentations of the lung cancer in tertiary level hospital, to observe and study the clinical and para-neoplastic manifestations of lung cancer and to identify reasons for delay in diagnosis of lung cancer in view of initial routine manifestations, as many cases in our country are diagnosed at stage III or IV.

DEMOGRAPHIC DETAILS

In the present study, mean age of the cases with lung cancer was 56.36 years and 30% of the cases were over 60 years of age. Most common associated co-morbidities were Type 2 Diabetes (21.77%), Hypertension (16.93%), COPD (11.29%) and Tuberculosis (8.06%).

Mean age reported by various authors is similar to present study as the disease is usually found in the older population because of prolonged exposure to risk factors. Among both women and men, the incidence of lung cancer is low in people aged <40 years and increases up to age 75–80 years in most population. Dubey N et al. reported the mean age of lung cancer was 58.6 yr. Charles S et al. reported it to be 57 years.

Male predominance was seen in present study with 63% males to 36% females which is in accordance with the GLOBOCAN 2018 report, males predominate with a male: female ratio of 4.5:1 has been reported. This is also seen in other Indian studies conducted by Prasad et al [6] and Jindal and Behera [7], Bhaskarapillai and colleagues [8] and Sheema Sheikh et al. [9], all have reported male predominance in their studies. In contrast to present study, Belcher JR found that in USA and UK, the male: female ratio was approximately 5:1 in 1970 but fell to around 2.5:1 in 1982 and Freedman ND et al. has reported that in the 40 years since, women's risk has risen markedly, becoming nearly iden tical to that of men. This is because of the striking increase in cigarette smoking in western women.

History of smoking was given by 59% cases while passive smoking and biomass fuel exposure was seen in 11% & 9% patients. Dubey N et al. also found that besides the tobacco smoke there was no significant exposure to any other carcinogenic substance except in female patients who were exposed to chulha smoke and environmental tobacco smoke at home. Majority of the patients were 'Bidi' smokers in their study.

Smoking as the most important risk factor for lung cancer in study, is also reported by Rawat et al.[10], Kumar et al. [11] and Koul et al. [12].

PRESENTING COMPLAINTS

This study revealed that lung cancer shares the common sympt om atology as other respiratory diseases. The most common presenting symptoms observed was cough (22.21%), chest pain (16.13%), fever (14.37%) and dyspnoea (11%) followed by hemoptysis (5.22%). Our findings are similar to study by Behera D et al., Vishwanath et al and Agarwal A in terms of complaints. They had also reported unexplained cough of several weeks as the commonest symptoms along with fever, weight loss, chest pain, and shortness of breath. It is also similar to some other reports published in the literature from different part of India. Cough is an early symptom due to bronchial irritation.

Association between COPD and lung cancer has been reported in numerous studies and is independent of patient's age and extent of tobacco smoking. Risk of lung cancer in a patient with COPD is 2-5 fold more as compared with smoker without COPD.

GENERAL PHYSICAL EXAMINATION

On general examination, lymphadenopathy and clubbing was observed in 16% and 19% cases while pallor and cachexia was seen in 12% cases and 6% cases each respectively. A study conducted by NC Purandare observed significant association between mediastinal, cervical, supraclavicular lymphadenopathy with lung cancer. Most common site of metastasis was the lymph nodes but the most common site for extra thoracic organ metastasis was the liver. Lymph nodes are also reported as commonest site of metastasis in studies by Arora et al. [14], Rajesekaran et al. [20] and Jindal and colleagues [21] and if evaluated can give us earliest diagnosis. In our study we have observed 16% patients with lymphadenopathy, which is statistically significant number.

On respiratory system examination, majority of the patients had clinical findings suggestive of pleural effusion (28%) (ie. fullness of intercostal spaces, absent breath sounds, stony dull note on percussion, etc) and obstructive airway disease (11%) (Unilateral or bilateral wheeze with or without prolonged expiratory phase of respiration). Clinical findings suggestive of consolidation were seen in 8% and that of lobar collapse in 4% of study population.

PARA-NEOPLASTIC SYNDROME

Para-neoplastic syndromes are a group of clinical disorders that are associated with malignant diseases and are not directly related to the physical effects of the primary or metastatic malignancy. Although para-neoplastic syndromes can be associated with many types of malignancies, they are most frequently associated with lung cancer.

A wide range of para-neoplastic syndromes were observed among our patients. Haematological manifestations like anemia, leucopenia and thrombocytopenia was seen in 20% cases while neurologic manifestations were seen in 8% cases. Paraneoplastic CNS manifestations observed were encephalopathy, peripheral neuropathy, transverse myelitis, cerebellar ataxia and opsoclonus. Other common para-neoplastic syndromes were SIADH and hypercalcemia, seen in 6% cases each.

The severity of anemia in these patients is dependent on disease stage, as well as the duration, type, and intensity of chemotherapy. Various studies across the India have reported high incidence of anemia in their studies. Kosmidis P et al and Kasuga I et al have studied anemia profile in a patients with lung cancer. Incidence of anemia in a lung cancer is as high as 100%, ranging from 20 - 100%.

Paraneoplastic neurological syndromes (PNSs) are neurological disorders caused by the remote effects of cancer and are not caused by the tumour itself, its metastasis, infection, ischemia or metabolic disruption. Dasgupta A et al. Reported neurological manifestations in 5 to 10% of cases of lung cancer which is in accordance to the present study. Another study of Sculier JP, et al. of 641 patients found that 29.5% had at least one neurologic disorder, either at the time of presentation or during the subsequent clinical course of the disease.

In DM associated with lung cancer, the common histological types were SCLC (29%) and squamous cell carcinoma (21%). PM/DM associated with lung adenocarcinoma appears to be rare. Present study observed 2% of dermatomyositis associated with lung cancer.

Squamous cell carcinomas was seen to be significantly associated with males and history of smoking in the present study. Adenocarcinomas were more common in females. We did not observe significant associations between histological form of cancers and para-neoplastic syndrome. The pattern of lung cancer has been changing in the West. Lung cancer is being increasingly diagnosed in women and adenocarcinoma has over taken SCC as the most common histological cell type. Kaur H et al. also observed similar findings in their study, they observed a significant association between quantified smokers, males and squamous cell carcinomas, the relation of squamous cell carcinomas to smoking has been proven by various other Indian studies and present study is in accordance with them.

The commonest radiological finding seen in present study was consolidation and pleural effusion. The adenocarcinoma commonly manifested as peripheral mass or a malignant pleural effusion. Similar finding were also reported in other studies. The SCLC presented commonly as central lesion, which was in agreement with other studies.

CONCLUSION

Lung cancer is emerging as a big medical and social problem for our country especially with rampant use of tobacco despite legislation to control it. Primary lung cancer should always be suspected in a person presenting with unexplained cough of more than 3 weeks with other symptoms such as weight loss, chest pain and fever. Most of the patients present at late stages of cancer, thereby causing delay in diagnosis, leading to an increase in fatal outcomes.

This study highlights the myriad clinical presentations of lung cancer among Indian patients. The key limitation of the current study is the relatively smaller sample size, and further studies are needed with larger sample size to better understand it.

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