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Prospective Study of Metastatic Lung Cancer Patients

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Abstract: ***Background: Worldwide cancer is becoming leading cause of death. Cancer incidence and mortality are rapidly growing worldwide. Among men prostate and lung cancer are the most frequently diagnosed cancers. Among males lung cancer is the leading cause of death in most countries. Materials and Methods: This was a prospective observational study done at Apollo Gleneagles Hospital, Kolkata in Department of Medical Oncology. Clinical and treatment details of all consecutive patients with metastatic lung cancer who underwent treatment at our center between August 2017 to July 2019 were collected and analyzed. A total of 54 patients were registered in the study. Results: Non-small cell lung cancer (NSCLC) patients comprised 50 and small cell lung cancer (SCLC) patients comprised 4 out of them. Median age was 56 years for NSCLC and 62 years for SCLC. Among NSCLC, adenocarcinoma was the commonest histological sub type. Males were 64% and female 36% of all NSCLC, while all SCLC patients were males. Conclusions: This study was conducted to know the demographic characteristics, histopathological and molecular characteristics, treatment pattern and outcome of metastatic lung cancer patients. Prevalence of EGFR mutation in non-small cell lung cancer was lower than expected and outcome of treatment was poor.***

Keywords: Lung cancer -prospective study - pathology review - survival – India

1. Introduction

Lung cancer is one of the commonest cancers and cause of cancer related mortality worldwide. According to estimates from the WHO in 2015, cancer is the first or second leading cause of death, before age 70 years in 91 of 172 countries; and it ranks third or fourth in additional 122 countries. Cancer incidence and mortality are rapidly growing worldwide. Among men prostate and lung cancer are the most frequently diagnosed cancers. According to Globocan 2018 data total number of new lung cases was 2093876 and total number of death due to lung cancer was 1761007. (1) Among males lung cancer is the leading cause of death in most countries. Incidence rate among male generally low in Africa and high in most developed countries and developing countries as well. In females too, lung cancer is one of the leading cause of cancer death in most countries. Incidence of lung cancer reflects the prevalence of smoking and pattern of lung cancer attributable to the type of smoking. The change in smoking pattern has led to increased diagnosis of adenocarcinoma compared to squamous cell carcinoma. 55% of non-small cell lung cancer is diagnosed in advanced stages.(2) 66% of patients with small cell lung cancer are diagnosed in advanced stages. Traditionally, palliative chemotherapy has been the standard of care for metastatic lung cancer. Many patients are unable to receive chemotherapy because of poor performance status. Recent advances in molecular testing and targeted therapy have changed the treatment approach for advanced stages of lung cancer. Challenges in diagnostic and molecular testing are availability of image guided biopsy and obtaining enough tissue for testing EGFR mutation, ALK-translocation and ROS-1 translocation. Immunotherapy has also been added as a treatment modality in recent times, which improves the prognosis considerably. Cost is another barrier for these newer modalities of treatment.

2. Materials and Methods

This was a prospective observational study done at Apollo Gleneagles Hospital, Kolkata in Department of Medical Oncology. Clinical and treatment details of all consecutive patients with metastatic lung cancer who underwent treatment at our center between August 2017 to July 2019 were collected and analyzed. A total of 54 patients were registered in the study.

Inclusion criteria

- Newly diagnosed metastatic lung cancer cases (stage IV according to AJCC 7th classification)
- Patient willing to give informed consent.
- Age greater than equal to 18 years.

Exclusion criteria:

- Those who already received chemotherapy or targeted therapy elsewhere.
- The study was approved by the Institute Ethics Committee.

Never-smokers were defined as those who had smoked fewer than 100 cigarettes during their lifetime; ever smokers were defined as those who had smoked 100 cigarettes or more during their lifetime. Diagnosis was established by core needle biopsy/ fine-needle aspiration cytology/body fluid cytology. Histopathologic examination and immunohistochemistry were done as appropriate. Molecular study for EGFR, ALK, ROS1 was done for adenocarcinoma histology while PDL1 was done as per physician's discretion.

Statistical Analysis

Statistical analysis was performed with help of Epi info(TM) 7.2.2.2. Epi Info is a trademark of Centers for Disease Control and Prevention(CDC).

Descriptive statistical analysis was performed to calculate the means with corresponding standard deviations(s.d).Test of proportion was used to find the Standard Normal Deviate(Z) to compare the difference proportions and Chi-square($\chi 2$) test was performed to find the associations. $p<0.05$ was taken to be statistically significant. Kaplan Meier method was used to evaluate the survival estimate.

3. Results

This study included total 54 patients. Non-small cell lung cancer (NSCLC) patients comprised 50 and small cell lung cancer (SCLC) patients comprised 4 out of them. Median age was 56 years for NSCLC and 62 years for SCLC. Among NSCLC, adenocarcinoma was the commonest histological sub type. Males were 64% and female 36% of all NSCLC, while all SCLC patients were males (Table 1)

Table 1: Demographic Features

Characteristics		NSCLC n =50(92.59%)	SCLC n=4(7.40%)
Age (years)	Median (range)	56(46-80)	62(40-72)
	41-50	5 (10%)	1 (25%)
	51-60	24 (48%)	1 (25%)
	61-70	15 (30%)	1 (25%)
	>70	6 (12%)	1 (25%)
Sex	Male	32 (64%)	4 (100%)
	Female	18 (36%)	0 (0%)
Smoking	Smoker	29 (58%)	2(50%)
	Non-smoker	21(42%)	2 (50%)
Pathological subtype	Squamous cell carcinoma	15(30%)	
	Adenocarcinoma	35(70%)	
	Small Cell Carcinoma		4 (100%)
Performance status (ECOG)	≤2	47 (94%)	4 (100%)
	>2	3 (6%)	0 (0%)

Diagnosis of lung cancer was confirmed by trucut biopsy in 68.51% patients and by FNAC in 18.51% patients (Table 2). Other patients were diagnosed by various cytology samples.

Table 2: Distribution of diagnostic modalities

Method of Diagnosis	No. of patients	% of Patients
Biopsy	37	68.51
Fine Needle Aspiration Cytology	10	18.51
Fluid cytology	5	9.25
sputum	1	1.85
Bronchoalveolar lavage	1	1.85

Treatment

Among 46 NSCLC patients who were treated with systemic therapy, 43 (93.4%) received first line chemotherapy. Two (4.3%) patients received first line EGFR inhibitor and one (2.2%) patient received ALK inhibitor as first line treatment (Table 3). Four patients received best supportive care alone.

Table 3: First line treatment for Non Small Cell Lung cancer

Treatment modality for 1st line therapy in NSCLC	No. of patients (n=46)	% of Patient
1st line chemotherapy	43	93.4
1st line Immunotherapy	0	0.0
1st line Chemo + Immunotherapy	0	0.0
EGFR Inhibitor	2	4.3
ALK Inhibitor	1	2.2

4. Discussion

In case of squamous cell carcinoma of lung, gemcitabine-platinum or taxane-platinum remain the preferred chemotherapy regimens. These regimens were almost equally distributed in our squamous cell carcinoma patients.

After first line chemotherapy response in NSCLC patients, partial response was observed in 25 (54.34%) patients, stable disease was in 11(23.91%) patients and 4 patients did not come for response assessment. We did not have enough patients to evaluate efficacy of individual regimens.

We found positive epithelial growth factor receptor (EGFR) mutation in 12%. This is lower than the other studies performed in India. Doval et al reported EGFR positivity in 33%.(22) Approximately 4% of patients in our study tested positive for anaplastic lymphoma kinase (ALK) translocation. This is comparable to results from other centres (2.7% to 3%) in India. In EGFR mutated patients, most of the studies published had first-generation TKI as the first-line therapy. In majority of the retrospective analyses as well as the randomized trials in these patients in the Indian context, the PFS and OS were higher than EGFR wild type. We had only 3 patients with EGFR mutation and one patient with ALK translocation. After first line TKI in NSCLC patients, partial response was observed in 1 (25%) patient and stable disease was observed in 1 (25%) patient. Because of small numbers of patients we could not generate meaningful estimate of PFS and OS in these patients.

After first line chemotherapy in SCLC patients, partial response was observed in 3 (75%) patients and disease progressed in 1 patient (25%).

Limitations of our study include small sample size, heterogeneity of regimens used, short duration of follow up and no use of immunotherapy in first line therapy. Molecular testing and PDL1 testing also could not be done in all patients.

In conclusion, there is a paradigm shift in the clinico-pathological profile of lung cancer in India. Despite recent advances in diagnostics and treatment, outcome of these patients still remain poor in real-world setting.