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Research Paper

Patients Profile, Pattern of Presentation and Response Rate to First Line Chemotherapy in Iraqi patients with Extensive Stage Small Cell Lung Cancer

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ABSTRACT:

BACKGROUND:

Lung cancer is the leading cause of cancer death worldwide, it comprises small cell and non-small cell subtypes. Small cell lung cancer carries a poorer prognosis, and it is mainly caused by cigarette smoking.

OBJECTIVE:

To assess response rate of extensive stage small cell lung cancer to first line chemotherapy and assess patient profile with pattern of presentation in Iraqi patients.

METHOD:

A cross-sectional study for small cell lung cancer patients who were treated at oncology teaching hospital, from January 1st 2020 to September 30th 2020 and included 30 patients with extensive stage small cell lung cancer.

RESULT:

Sixty patients with small cell lung cancer were interviewed, 30 patients of them were included in this study. The mean age of the patients was 58.27±9.71years. Males represented more than three quarters of the patients (76.67%). The male female ratio was 1:0.3. The mean weight, height and body mass index of the patients were 67.2±12.52 kg, 168.93±8.8 cm and 23.48±3.58 kg/m2, respectively. Almost all patients were either ex-smokers or current smokers. Cough was the most common presentation encountered in 11 patients (36.67%). Eight patients (26.67%) showed no response to the treatment, while 22 patients (73.3%) had clinical benefit of which 10 patients (33.33%) were stable, 10 patients (33.33%) had partial response and two patients (6.67%) had complete remission. Mean progression free survival time was 6.71±1.5 months, 95%CI= 5.83-7.6. After three months, in 8 patients (26.67%) the disease progressed, while almost all other patients had progression free survival till 7-9 months after treatment.

CONCLUSION:

Extensive stage small cell lung cancer is an aggressive disease that is chemosensitive but rapidly progressive in Iraqi patients. It is adherent to tobacco exposure with male to female ratio of 1:0.3. Affected population is mostly middle age group, presenting with cough.

KEYWORDS: Small Cell Lung Cancer, Extensive Stage, Response Rate.

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INTRODUCTION:

Lung cancer is the first leading cause of cancer-related-death worldwide [1-5]. In 2020, Siegel et al., documented 228,820 new cases of lung cancer and 135,720 deaths [6]. Only 19% of all cases with lung cancer are survival five-years after initial diagnosis [7].

In 2019, 29,660 new cases of SCLC would be reported in the USA [8]. In Iraq, it accounts for 7.5% of all cancer cases second to breast cancer only, as documented in Iraqi cancer registry 2020 [9].

Almost all cases of are cigarette smoking etiology [10]. The SCLC incidence has been dropping, while the incidence in females raising recently and the M:F ratio is 1:1 today [8]. SCLC is rapidly doubling time, have high growth fraction and early cause of cancer-related-death in the US [5].

Most patients with SCLC exposed to hematogenous metastases; as one third complained of limited disease. This stage is very sensitive to chemotherapy agents and radiotherapy fractions; however, most cases

eventually dying due to recurrence [11]. In limited-stage, the goal of management is cure; some patients are eligible for curative surgery followed by systemic therapy with or without radiation to the mediastinum [11-13].

The extensive-stage disease, systemic therapy used to palliate symptoms and may be prolongation of the survival; however, the survival mostly rare [14]. Surgery is recommended for cases with re-sectable stage I – IIA. Stereotactic ablative radiotherapy (SABR) is recommend for inoperable cases with stage I - IIA [15-18].

Poor performance status (PS) (3–4), weight losing, extensive-stage diseases, high level of markers as LDH and bulky disease are adverse prognostic indicators. Female, younger, normal LDH, and stage I tumor are the favorable prognostic indicators in limited-stage disease. Younger, good performance, normal creatinine and LDH levels, and oligo metastatic lesion are favorable prognostic indicators in extensive-stage diseases [19, 20].

In one study, response rates of ES to first line chemotherapy EP is 64%.and the median overall survival 10.3 months [95% CI, 9.3–11.3]). The 1-year overall survival rate 38.2% (hazard ratio [HR] for death, 0.7 [95% CI, 0.54– 0.91; P = .007]) [21].

This study aimed to assess response rate of extensive stage small cell lung cancer to first line chemotherapy and assess case profile with pattern of presentation in Iraqi patients.

PATIENTS AND METHODS:

Study design & settings

A cross-sectional study, on patients with lung cancer who attended Oncology Teaching Hospital, from January 2020 to September 2020.

Participants

Computed tomography (CT) scan assessment done with dynamic intravenous contrast (oncology protocol: chest, abdomen and pelvic CT) plus brain MRI (magnetic resonance imaging) before & after the treatment.

Inclusion criteria

- Extensive stage disease
- Normal brain MRI
- Good performance status (ECOG score 0-1)
- Written consent

Exclusion criteria

- Limited stage disease
- Poor performance status (ECOG score >1)
- History of another primary malignancy
- Liver impairment
- Renal impairment
- Non - compliance to treatment

Ethical considerations

The Scientific and Ethical Committee (SEC) of Iraqi Board of Medical Specialties (IBMS) approved this study. Data from medical records were collected after agreement of health authority at Oncology Teaching hospital in Baghdad.

Clinical examination and data collection

History and clinical examination was done for all the patients and data were collected including: age, BMI, smoking history, radiation history, drug history, performance status, histopathologic type of cancer and TNM staging.

Follow up and assessment

For assessment of response rate, we use revised RESCIST criteria version 1.1:

- **Complete Response (CR):** Disappearance of all target lesions.
- **Partial Response (PR):** At least a 30% eliminate of diameters of lesions.
- **Progressive Disease (PD):** At least a 20% elevate of diameters of lesions.
- **Stable disease (SD):** Neither sufficient shrinkage nor sufficient increase to qualify for PD [22].

Data analysis

All statistics were analysed by IBM SPSS v. 19.0 (IBM, Armonk, NY, US). Quantitative variables were expressed as mean±standard deviation and as range, while discrete variables were described as number and percent. A p-value of less or equal to 0.05 was considered significant.

RESULTS:

Demography of patients

Sixty patients with SCLC were interviewed, 30 patients of them were included in this study. The mean age of the patients was 58.27±9.71years (range 42-74 years). Males represented more than three-quarters of the patients (76.67%). The male female ratio was 1:0.3. The mean weight, height and BMI of the patients were 67.2±12.52 kg, 168.93±8.8 cm and 23.48±3.58 kg/m2, respectively. Almost all patients were either ex- or current smokers. In about one-third of the patients, the ECOG was zero, while it was 1 in the other two-thirds, (Table 1).

Table 1: Demography of the patients (No.=30).

Variables	Values
Age (years)	
Mean±SD	58.27±9.71
Range	42-74
Gender	
Male	23(76.67%)
Female	7(23.33%)
Weight, kg	
Mean±SD	67.2±12.52
Range	59-89
Height, cm	
Mean±SD	168.93±8.8
Range	150-179
BMI, kg/m^2	
Mean±SD	23.48±3.58
Range	18.69-32.69
Smoking	
Never	1(3.33%)
Ex/current smokers	29(96.67%)
ECOG	
Zero	11(36.67%)
One	19(63.33%)

Therapeutic and Clinical Characteristics of the Patients

Out of 30 patients involved in the study, 12 (40%) had a type of comorbidity, while the other 60% had not. The most common comorbidity was hypertension accounting for 36.57% of patients. Type 2 diabetes mellitus was less common and was encountered in 10% of the patients. Cough was the most common presentation encountered in 11 patients (36.67%) followed dyspnea (30%) and chest pain (10%). Less commonly, two patients (6.67%) presented with loss of weight. The vast majority of patients (86.67%) received 6 cycles treatment (Table 2).

Table 2: Therapeutic and clinical characteristics of the patients (n=30).

Variables	Frequency (%)
Comorbidities No comorbidity Hypertension Diabetes mellitus	18(53.33) 10(36.57) 3(10)
Presentation	
Cough	11(36.67)
Dyspnea	9(30)
Chest pain	3(10)
Hemoptysis	4(13.33)
Loss of Weight	2(6.67)
Treatment cycles	
4	4(13.33)
6	26(86.67)

Response to treatment

Out of 30 patients included in the study, 8 patients (26.67%) showed no response to the treatment, while 22 patients (73.3%) had clinical benefit of which 10 patients (33.33%) were stable, 10 patients (33.33%) had partial response and two patients (6.67%) had complete remission (Figure 1).

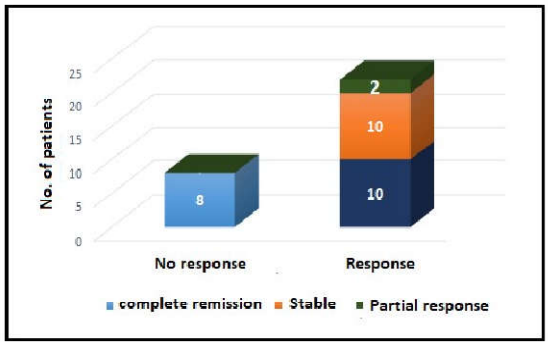

Figure 1: Responsive and non-responsive patients

Progression Free Survival

Mean PFS time was 6.71±1.5 months, (95%CI= 5.83-7.6). After three months, in 8 patients (26.67%) the disease progressed, while almost all other patients had PFS till 7-9 months after treatment (Figure 2).

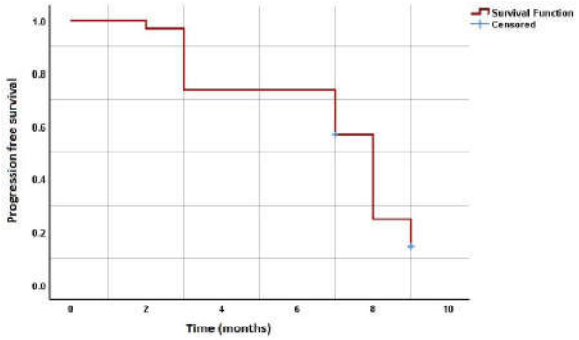

Figure 2: Kaplan Meier curve for PFS

DISCUSSION:

Small cell lung cancer is an aggressive disease mainly caused by cigarette smoking as shown by this study being associated with 96% (29 of 30) of all patients which is comparable to global studies such as Pesch et al, [23] study which was a large study conducted in Europe and Canada in 2012, found that tobacco exposure is a causative agent for 97% of SCLC cases. This meta-analytic study involved 13,169 patients and 16,010 healthy subjects from Canada and Europe. Male smokers consuming an average of 30 cigarettes a day had Age-adjusted odds ratios of 103.5 for squamous cell carcinoma, 111.3 for SCLC and 21.9 for Adenocarcinoma. The corresponding Age adjusted odds ratios in women were 62.7, 108.6 and 16.8, respectively [23].

But unlike the statistics in western countries, male to female ratio in this study is 1:0.3 (23 males versus 7 females) as compared to 1:1 ratio in USA according to Govindan et al, [24] which there was high male-to-female ratio in small cell lung cancer patients in 1973 has declined over the next twenty years steadily. In 2002, the M:F ratio was 1 to 1. That may reflect decreased ratio of females' tobacco exposure versus males' tobacco exposure in Iraq compared to its ratio in USA [24]. The affected age group in this study is mainly middle aged people which is comparable to Jemal, et al, [25] and Früh et al, [26].

The presenting symptoms in this study are cough, dyspnea and chest pain is comparable to study of Winston et al, [27].

The objective response rate to first line chemotherapy in this study is 73% where 8 patients (26.67%) showed no response to the treatment, while 22 patients (73.3%) had clinical benefit of which 10 patients (33.33%) were stable, 10 patients (33.33%) had partial response and two patients (6.67%) had complete remission. As compared to 62.69% shown by 2 meta analyses conducted by Pojol et al, [28] in Cancer Research UK in 2000. Where identified

of 19 studies previously published. Ten trials randomized cases used Etoposide-Cisplatin regimen vs. arm without anti-cancer agent. A subgroup analysis conducted in the 9 rest studies that were randomly allocated cases between two arms differing in the presence or absence of Cisplatin, while Etoposide given or not in both regimens. Cases randomized in a Cisplatin contain regimen had an elevate in response rate [28].

Progression free survival is 6.71±1.5 months in this study where after three months, in 8 patients (26.67%) the disease progressed, while almost all other patients had PFS till 7-9 months after treatment compared to 8-9 months at a retrospective study of Merseyside and Cheshire Cancer network by Sallam et al, [29] in Liverpool UK in 2019. Where 241 cases stage IV disease had four cycles and 69 cases had more than four cycles. There were no differences in clinical outcomes comparison. The median duration of response was 5 months in both groups median PFS was eight months (four cycles) versus nine months (more than four cycles) [29].

CONCLUSION:

Extensive stage small cell lung cancer is an aggressive disease that is mostly chemosensitive (73% response rate to first line chemotherapy) but rapidly progressive (Mean progression free survival is 6.7 months) in Iraqi patients. It is adherent to tobacco smoking with male to female ratio of 1:0.3 which mirrors smoking pattern in Iraqi patients. Affected population is mostly middle age group presenting with cough and dyspnea.

Recommendations

Advice of smoking cessation by health education and by activating programs of smoking cessation and banning of smoking in public places and hospitals. Encouraging patients and doctors to participate in clinical trials of SCLC management. We need more time and a larger sample to evaluate the outcome of the disease in the form of response rate to treatment and the progression free survival.

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