Impact of Radiotherapy in Small Cell Carcinoma of Lung

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ABSTRACT

BACKGROUND: Small cell carcinoma of lung has a drastically different and an aggressive natural history with its rapid growth and early systemic spread. Despite its chemo-sensitivity, it has an exquisite tendency for local recurrence. There is irrefutable evidence that addition of radiotherapy can achieve excellent local control within its treatment portals.

OBJECTIVE: To evaluate the role of radiotherapy in small cell carcinoma of lung.

METHODS: 55 cases of small cell carcinoma of lung were treated in the Department of Radiotherapy from Jan, 1996 to Dec, 2000. Four subsets of patients were analysed with all medical records and follow-up. Group-I included cases who had not received any specific treatment. Group-II had received chemotherapy alone. Group-III had received chemo-radiotherapy and Group-IV had undergone surgery followed by chemo-radiotherapy.

RESULTS: Overall survival at 1, 2 and 3 year follow-up was 15.3%, 13.2% and 7.8% in cases who had received radiation in addition to chemotherapy. There were 2 cases (3.7%) in Group-IV who had 5 year survival.

CONCLUSION: Addition of radiotherapy to chemotherapy protocols has an important role in improving the survival in this type of lung cancer. JMS 2010;13(2):60-63

Key words: Small cell lung cancer, chemotherapy, radiotherapy

Small cell lung cancer (SCLC) differs from other histological types of lung cancer in its rapid growth and propensity for early and wide spread metastasis.¹ It accounts for about 20-25% of newly diagnosed lung cancer cases in the world and has an aggressive clinical course.^{2,3} In Kashmir valley, small cell lung cancer constitutes nearly 17% of all lung cancers.⁴ In contrast to other main histological types of lung cancer, small cell carcinoma is generally non-resectable but highly sensitive to both chemotherapy and radiotherapy.⁵ Despite excellent response to aggressive induction chemotherapy, small cell lung cancer has an exquisite tendency to

recur in areas of original involvement, particularly in the chest.⁶ There is irrefutable evidence that small cell lung cancer is highly responsive to radiation therapy and that this modality can achieve excellent local control within its treatment portals.⁶ Several meta-analysis confirmed the efficacy of the addition of thoracic irradiation to chemotherapy in limited disease small cell lung cancer and demonstrated a 5% improvement in 3 year survival and 25% improvement in local tumor control.^{7,8} Radiotherapy plays an extremely important role in palliation of symptoms of the primary tumor and metastatic disease in extensive stage disease.² Despite the advances in the management of lung cancer in general, small cell lung cancer still poses a challenge to the oncologists. Five year survival, the traditional benchmark for cure in most cancers, occurs in only 4% of patients with small cell lung cancer.^{9,10} This study was undertaken to determine the role of radiation therapy in the management of small cell lung cancer.

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Methods

We reviewed the Departmental records of all patients treated at our tertiary care hospital between 1996 and 2000 with the diagnosis of small cell lung cancer. Cases that had full medical records with a minimum follow up of 3 months were included. Patients with incomplete medical records and or incomplete treatment were excluded from the study. All patients had histological or cytological confirmation of small cell lung cancer determined through bronchoscopy, fine needle aspiration or open biopsy. All patients had undergone staging workup in the form of history, physical examination, complete blood count, biochemistry, CT scan of chest and brain, bone scan, ultrasonography besides the chest radiography. A total of 55 patients were included for analysis of outcome of various treatment strategies. Of these 21 patients had extensive stage and 34 had limited stage disease. On the basis of treatment, patients were divided into four groups. Group-I (17 cases) included those patients who had not received any specific treatment and were on symptomatic treatment only. These patients had either extensive stage (9 cases) and or refused treatment (8 cases) because of the poor performance and poor socio-economic status. Group- II (16 patients) included cases who were treated with chemotherapy alone. Group-III (16 cases) were treated with chemo-radiotherapy and Group- IV (6 cases) had undergone surgery followed by chemo-radiotherapy. Chemotherapy was given in the form of inj. Cisplatin, 50mg/m² i/v infusion over 3 hours per day for 3 days, after adequate hydration and premedication, Inj. Etoposide, 100mg/m² i/v infusion over 2 hours for 3 days. Cycle was repeated after 3 weeks. Radiation was delivered on cobalt-60 teletherapy unit (Theratron-780). The radiation field included the gross disease as seen on chest x-ray with 2-3cm margin, the mediastinum and ipsilateral hilum. Supraclavicular areas were included in treatment field in case of the disease in upper lobes. Treatment was delivered by antero-posterior parallel opposed portals. A radiation dose of 45 Gy was delivered in 20 fractions with five fractions in a week. Surgery was done in the form of open biopsy/lobectomy. The sequence of treatment in this group was surgery followed by 3 cycles of chemotherapy followed by radiotherapy followed by 3 more cycles of chemotherapy. Follow-up of 3 months to 5 years was available. Prophylactic cranial irradiation (PCI) was not used. Patients lost to follow-up were considered dead.

Results

From January 1996 through December 2000, fifty-five patients with small cell carcinoma of the lung were studied retrospectively. Patient characteristics are shown in Table 1. There were 50(90.9%) male and 5(9.1%) female patients in the age group ranging from 30 to 80 years (median 53 years); 31(56.4%) patients were from rural and 24 (43.6%) from urban areas. Out of 55 patients 37(67.3%) were active smokers, and 18(32.7%) had no history of smoking. All

Table 1: Distribution of patients according to various clinical & demographic parameters (n=55)

Variable	N*	Percent
Median Age (years)	53	
Sex		
Male	50	90.9
Female	5	9.1
Habitat		
Rural	31	56.4
Urban	24	43.6
Smoking History		
Smokers	37	67.3
Non-Smokers	18	32.7
Site of involvement		
Right Lung	31	56.4
Left Lung	24	43.6
Bronchoscopy		
Positive	40	72.7
Negative	15	27.3

*Number, unless specified

patients had undergone bronchoscopy of which 40(72.7%) had positive diagnostic yield, and 15(27.3%) had negative yield. These 15 patients were diagnosed with the help of trucut biopsy (8 cases), thoracotomy (2) and FNAC of supra-clavicular lymph node (5 cases). As per the bronchosopic and chest radiographic findings, 31(56.4%) had lesion in the right lung and 24 (43.6%) had in the left lung. Of the 55 patients, 38 received chemotherapy of which 7 had received six cycles, 10 had received 4 cycles while as 21 patients had received 3 or less cycles of chemotherapy. Grade I and II chemotherapy toxicity was observed in 11 cases and grade III toxicity in 4 cases. Majority of cases did not complete full chemotherapy mainly because of socio-economic reasons. Of the 55 patients 30 patients were planned for radiotherapy and only 22 had completed the prescribed dose of radiation i.e., 45 Gy/20 fractions/4 weeks, (Group- III & IV). Out of the six patients who had undergone surgery, two had inoperable growth at thoracotomy and in 4 patients lobectomy was performed. During the treatment and subsequent follow-up, 7 patients developed metastasis, 5 in bone (dorsal spine), one in brain and one in liver. The overall survival at 1 year, 2 year and 3 years was 15.3%, 13.2% and 7.8% respectively (Table 2). This excludes patients in Group-I, who had not received any specific treatment. As per the treatment, long survival of 5 years was seen in Group- IV followed by Group- III.

Table 2. Distribution of cases according to their overall survival

Follow-up	Group-I	Group-II	Group-III	Group-IV
3 months	9 (52.5%)	15 (93.7%)	16 (100%)	6 (100%)
6 months	-	10 (62.5%)	12 (75%)	6 (100%)
12 months	-	-	4 (25%)	2 (33%)
24 months	-	-	3 (18%)	2 (33%)
36 months	-	-	1 (6%)	2 (33%)
60 months	-	-	-	2 (33%)

Figure: Graphical representation of percentage survival of four groups of patients

Discussion

This retrospective study was undertaken to find out the role of radiotherapy in patients with small cell lung cancer. Surgery, radiotherapy and chemotherapy are the various options available for the management of lung cancer. Surgery is not considered as a part of standard treatment of small cell lung cancer due to its propensity for early spread.¹¹ Surgery as an option of treatment was discarded 30 years ago, when randomized study demonstrated better results with radiotherapy.² In the current study 2 out of 55 patients (3.7%) who had undergone surgery followed by chemo-radiotherapy were alive at 5 years of follow-up. This shows that surgery as a single modality has no role in small cell lung cancer, but when combined with chemo-radiotherapy, it definitely improves survival in a selected group of patients. Although, the chances of cure in small cell lung cancer are small, treatment is indicated in most cases, since the median survival is markedly increased from 2 to 3 months in untreated patients to 8 to 16 months in patients treated with chemotherapy.^{9,12} We also observed that Group I patients were lost to follow-up within three months and those who had received at least one modality of treatment (Group-II) 62.5% of patients were alive at 6 months (Table-2). Randomized trials have established that combination chemotherapy is clearly superior to single agent chemotherapy in small cell lung cancer.^{11,12} Treatment for limited disease SCLC includes combined modality in the form of thoracic radiation and systemic chemotherapy.¹³ Radiation is usually given either sequentially or concurrently with systemic chemotherapy.¹⁴ Pignon *et al* Collected data on 2140 patients from 16 randomized trials

comparing chemotherapy alone versus chemotherapy plus thoracic radiotherapy and found an improvement in absolute survival of 5.4% at three years.^{2,8} None of the cases received PCI. Even the 2 long term survivors were not given PCI. In limited stage group only one patient developed brain metastasis. Role of PCI in small cell carcinoma of lung has been controversial though it, no doubt, improves the Disease free survival and as such, at present, most of oncology centers use this in complete responders with early/limited stage disease.^{14a}

Perry *et al* first reported a survival advantage with addition of thoracic radiotherapy to chemotherapy in limited stage disease.¹⁵ We also observed that addition of radiotherapy in Group- III and IV has definitely improved survival when compared to Group-I and II (Table-2). This strongly justifies the role of radiotherapy in the management of small cell lung cancer irrespective of its stage. Our results are similar with those who reported survival advantage with addition of thoracic radiotherapy to chemotherapy in limited stage disease.^{8,16} However, in extensive stage disease, addition of chest irradiation to chemotherapy has reduced frequency of local recurrence, but did not alter the objective response rates, median survival or 2 year disease free survival.^{12,17} With current treatment protocols 5 year survival of 20-23% has been achieved in limited stage disease. However, our overall survival of the whole cohort was 3.7% and we had only 2 cases who survived 5 years. Poor outcome in our study was directly related to the advanced stage of disease, poor performance status, poor socio-economical status which leads to lot of drop outs and inadequate treatment.

In conclusion, Small cell lung cancer is an aggressive disease with a propensity for early dissemination. Radiotherapy plays a pivotal role for major therapeutic programs of this disease. Even with real benefit from radiotherapy, more effective chemotherapy programs need to be developed to deal with the systemic nature of the disease, if the outcome for patients with small cell lung cancer is to improve.

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