LEADING ARTICLE

# IMPROVING THE RESULTS OF SMALL CELL LUNG CANCER

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Small cell lung cancer (SCLC) or "oat cell" lung cancer represents 20-25% of all lung cancers. If left untreated, it is the most rapidly fatal form of lung cancer with a median survival of 6 to 20 weeks[1]. The disease is associated with a male predominance, rapid onset of symptomatology, paraneoplastic syndromes, central thoracic location, early metastasis, low resectability and 5 year survival of less than 1%. Prior to 1970, surgery and radiotherapy constituted the most commonly applied forms of treatment[2]. However, neither of these purely localised therapeutic modalities are capable of providing effective long term disease control in the majority of the patients. Appreciation of the frequency and extent of metastatic disease coupled with the sensitivity of SCLC to a variety of chemotherapeutic agents has subsequently led to the present emphasis on the central role of systemic chemotherapy in patient management[3]. These changes have resulted in a 4-5 fold prolongation of median survival. In this issue, a group of patients with limited and extensive stage SCLC was treated with combination chemotherapy producing very good response rate and survival.

A wide variety of chemotherapeutic combinations has been used in the past for the treatment of SCLC. There is no question that the use of multiple drugs is more effective, as far as response and survival are concerned, than single drug therapy[4]. Since many chemotherapeutic agents are active in SCLC, it is not surprising that the possibilities for combining these drugs are many. In this issue, the authors used cyclophosphamide, doxorubicin and vincristine as the chemotherapy programme. At present there is no standardised therapy for SCLC but most combination chemotherapy trials produce an overall complete response rate of 50% with limited disease and 30% in those with extensive disease. Nearly all trials show a remarkably consistent duration of survival. The median survival time was 14 months in patients with limited disease and about 9 months in those with extensive disease. Long term survivals were only seen in 10-15% of patients with limited disease[5].

The strategies of chemotherapy administration in SCLC are similar to the optimal methods of drug treatment in several adult cancers which can be cured with chemotherapy alone. Currently the active single agents for SCLC include cyclophosphamide, doxorubicin or its analogue, cisplatin, vincristine, etoposide and ifosphamide. Combination chemotherapy incorporating some of these agents is now the mainstay of treatment[6].

There are many questions which ongoing trials are trying to address. They include dose intensity, optimal number of drugs, autologous marrow transplantation, consolidation radiation to primary pulmonary lesion and prophylactic cranial irradiation. Many of these studies suggest that two or three drugs are optimal but dose intensity of initial chemotherapy is important. The principal toxicities produced by all combination chemotherapy programmes are those related to myelosuppression, specifically neutropenia-associated fever and infection and to a much lesser extent, thrombocytopenic bleeding. Patients with poor performance status or extensive-stage disease are at greater risk.

This neoplasm is the most responsive of all cell types of lung cancer to thoracic radiotherapy[7]. Thus chest irradiation in conjunction with chemotherapy may improve therapeutic results, particularly in patients with limited disease, appears logical. The results of combined modality suggest lower rate of local recurrence but patients have high haematologic, pulmonary and oesophageal complications.

Brain metastases are detected in approximately 10% of SCLC at the time of presentation and are subsequently diagnosed during life in another 20-25%. In most trials on prophylactic cranial irradiation, there is reduced risk of intracranial tumour spread but no significant impact on survival could be appreciated[8]. The current recommendation is to use prophylactic cranial irradiation only in patients who are complete responders using fractions of 200-300 cGy *to a total of 2400-3000 cGy* and avoid concurrent chemotherapy.

Though great strides have been made in the treatment of SCLC, there are many problems which prevent translation of the high response rates to high cure rates. The search to improve the present results of small cell lung cancer continues.

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