Europ. J. Cancer Vol. 16, pp. 1447–1450
© Pergamon Press Ltd. 1980. Printed in Great Britain

0014-2964/80/1101-1447 $02.00/0

Prognostic Value of the Superior Vena Cava Syndrome as the Presenting Sign of Small Cell Anaplastic Carcinoma of the Lung

P. VAN HOUTTE,*† R. DE JAGER,‡ J. LUSTMAN-MARÉCHAL* and Y. KENIS‡

*Service de Radiotherapie, Institut J. Bordet, 1 rue Héger-Bordet, 1000 Bruxelles, and ‡Service de Medecine et Laboratoire d'Investigation Clinique Henri Tagnon, Institut J. Bordet, 1 rue Héger-Bordet, 1000 Bruxelles, Belgium.

Abstract—*In a series of 45 patients with small cell anaplastic carcinoma of the lung with disease limited to one hemithorax, 15 of them presented at the time of diagnosis a superior vena cava syndrome. Both groups were similar in terms of response rate and survival. Superior vena cava syndrome is not an independent prognostic factor in small cell carcinoma of the lung.*

INTRODUCTION

OBSTRUCTION of the superior vena cava produces a dramatic syndrome (SVCS) which is associated in more than 90% of cases with a malignant tumor, and among these bronchogenic carcinoma accounts for 75% [1, 2]. The literature suggests that combination of SVCS and this cancer carries a worse prognosis in terms of survival despite symptomatic relief from treatment [3].

The incidence of SVCS was particularly high in a series of small cell anaplastic carcinoma of the lung treated by a combined modality: radiotherapy and chemotherapy [4]. The present study analyses the prognostic value of SVCS as presenting sign in small cell carcinoma of the lung.

MATERIALS AND METHODS

Between 1973 and 1978, 45 patients with biopsy proven small cell anaplastic carcinoma of the lung with limited disease were treated with a combination of radio- and chemotherapy. They fulfilled the following criteria: no prior treatment with surgery, radiotherapy or chemotherapy, no history of other malignant disease and age below 72 yr.

All cases were classified as limited disease after a staging procedure including chest X-ray, tomograms, fiberbronchoscopy, bone, brain and liver scintigraphies, bone marrow biopsy and peritoneoscopy with liver biopsies if possible.

Limited disease was defined as a tumor extension confined to one hemithorax, mediastinum and homolateral supraclavicular nodes.

The therapeutic regimen has been previously published [4]. The induction treatment consisted of two courses of chemotherapy at 3 weeks interval (vincristine 1.5 mg/m^2 i.v. days 1 and 8 and cyclophosphamide 1.2 g/m^2 i.v. day 1 (VCR-CPA) and radiation therapy (45 Gy through megavoltage equipment in $4\frac{1}{2}$ weeks to the primary tumor and the mediastinum).

Two weeks after the completion of radiation therapy maintenance chemotherapy was started for a period of 2 yr or until relapse. Patients received either 3-weekly courses of VCR-CPA or monthly courses of COMB (CPA 600 mg/m^2 i.v. and MeCCNU 80 mg/m^2 per os day 1, VCR 0.75 mg/m^2 i.v. and bleomycin 10 mg/m^2 i.v. on day 2).

The evaluation of treatment was performed at the beginning of the maintenance chemotherapy as follows: a complete response corresponded to a complete disappearance of all tumor lesions. Partial response corresponded to a decrease of more than 50% of the sum of the products of the two largest perpendicular diameters of all measurable lesions without appearance of other tumors. The acturial method of Kaplan–Meyer was used to establish the survival curves.

RESULTS

Fifteen patients out of 45 presented with superior vena cava syndrome (SVCS) at the time of diagnosis. Actuarial median survival was 11 months for the whole series. No differ-

Accepted 10 April 1980.

†Reprint requests and correspondence to be addressed to Dr. P. Van Houtte.

ence was observed between the entire group and patients with SVCS (Fig. 1). Seven patients survived more than 2 yr: 2 with SVCS and 5 without SVCS.

No difference in general was observed between 27 patients treated by COMB and 9 by VCR-CPA with a median survival of 11 months for both chemotherapies. Moreover the survival curves for patients with maintenance chemotherapy with COMB were identical in presence or absence of SVCS.

The treatment resulted in 80.2% of objective response. In all cases, a complete disappearance of SVCS signs was observed except for superficial veins on upper torso (Table 1). The most common sites of relapse were intrathoracic progression, bone and brain metastases (Table 2). An increase in brain metastases was observed for patients with SVCS; however, this difference did not reach a statistical level ($P=0.1$). The delay of occurrence was the same in presence or absence of SVCS.

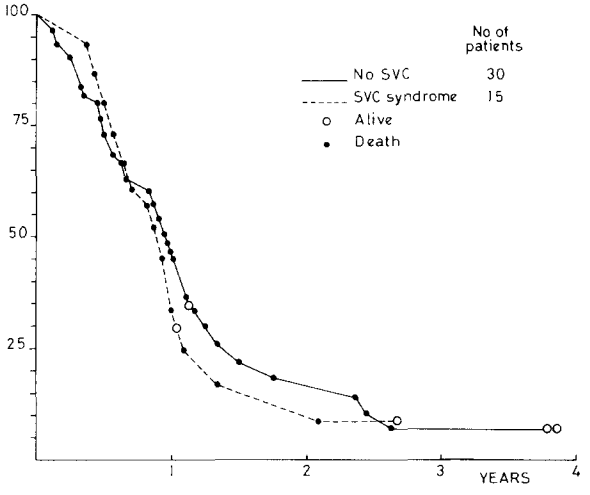

Fig. 1. Small cell carcinoma of the lung = limited disease influence of superior vena cava syndrome on survival.

Table 1. Small cell anaplastic carcinoma of the lung—therapeutic response

	Complete response	Partial response	No response	Not evaluable	Total
With SVCS	9	6			15
Without SVCS	10	12	7	1	30
Total	19	18	7	1	45
Response rate	37/45 (80%)				

Table 2. Small cell anaplastic carcinoma of the lung—site of relapse

	No SVCS	SVCS
Local	7	1
Thoracotomy scar	1	
Cervical nodes	1	1
Heterol. lung	1	
Brain	5	6
Liver	4	
Bone	3	3
Stomach	1	
Toxicity	1	
Unknown	4	?
	28/30	13/15

DISCUSSION

Today the most common cause of obstruction of the superior vena cava is represented by bronchogenic carcinoma which is responsible for 90% of all cases [1, 2, 5]. Other neoplastic causes are lymphoma, intrathoracic tumors such as thymoma, metastatic cancer [5]. Benign diseases account in 3–5% of cases for the onset of this syndrome including goiter, bronchogenic cysts, pericardial constriction, aneurysm, iatrogenic causes such as central venous catheter, irradiation induced pneumonitis [5, 6]. Thirty years ago, SVCS resulted in the same proportion from intrathoracic tumor or aortic aneurysm which is now a very rare etiology [7].

The combination of SVCS and bronchogenic carcinoma is particularly lethal: prolonged survival has been very rare in spite of the relief of symptom after radio- or chemotherapy. The overall 1 yr survival for all cell types is less than 5% [3, 8].

Small cell anaplastic carcinoma of the lung represents one third of all cases of SVCS due to lung tumor [5]. This tumor presents a particular behaviour characterized by a rapid and extensive mediastinal invasion and an early metastatic spread outside the chest [9]. This explains the failure of local and regional therapies in the management of this disease and the necessity of a systemic treatment [10]. Moreover, this cell type tumor presents a very high percentage of response to chemotherapy and radiotherapy [9].

Contrary to the classical statement, the presence of SVCS at presentation does not adversely affect the prognosis of patients with small cell anaplastic lung carcinoma treated with a combination of chemotherapy and radiotherapy. The relapse pattern shows a trend towards an increase in brain metastases for patients with SVCS; this syndrome may be a risk factor for such relapse and the use of prophylactic brain irradiation can be especially considered in such a situation.

The relief of symptoms observed after radiotherapy results either from an improvement of flow through collateral supply or due to a reduction of the obstructing tumor with an increase in blood flow through the vena cava. ^{99m}Tc Isoptopic phlebography can easily be performed and repeated without any risk for a patient with SVCS. In small series, the improvement after treatment was largely due to an increase in blood flow through the vena cava rather than in the collateral supply [11–13].

SVCS is not an independant prognostic factor in small cell anaplastic carcinoma of the lung.

REFERENCES

1. J. J. Lokich and R. Goodman, Superior vena cava syndrome, clinical management. *J. Amer. med. Ass.* **231,** 58 (1975).
2. P. Rubin, Symposium on superior vena cava obstruction: introduction. *Radiology* **81,** 377 (1963).
3. B. Roswit, G. Kaplan and E. G. Jacobson, The superior vena cava obstruction syndrome in bronchogenic carcinoma. *Radiology* **61,** 722 (1953).
4. P. Van Houtte, G. Tancini, R. De Jager, J. Lustman-Marcéchal, F. Milani, G. Bonadonna and Y. Kenis, Small cell carcinoma of the lung: a combined modality treatment. *Europ. J. Cancer* **15,** 1159 (1979).
5. R. J. Polackwich and M. J. Strauss, Superior vena cava syndrome. In *Lung Cancer—Clinical Diagnosis and Treatment* (Edited by M. J. Strauss). Grune & Stratton, New York (1977).
6. V. Mahajan, V. Strimlan, H. Van Ordstrand and F. D. Loop, Benign superior vena cava syndrome. *Chest* **68,** 32 (1975).
7. F. T. McIntire and E. M. Sykes, Obstruction of the superior vena cava: a review of the literature and report of two personal cases. *Ann. intern. Med.* **30,** 925 (1949).
8. P. Rubin, J. Green and G. Holzwasser, Superior vena cava syndrome. *Radiology* **87,** 388 (1963).
9. L. E. Broder, M. H. Cohenand and O. S. Selawry, Treatment of bronchogenic carcinoma. II. Small cell. *Cancer Treat. Rev.* **4,** 219 (1977).
10. W. Fox and J. G. Scadding, Medical Research Council comparative trial of surgery and radiotherapy for primary treatment of small celled or oat-celled carcinoma of bronchus. *Lancet* **ii,** 63 (1973).
11. Y. H. Son, R. A. Wetzel and W. J. Wilson, ^{99m}Tc pertechnate scintiphotography as diagnostic and follow-up aids in major vascular obstruction due to malignant neoplasm. *Radiology* **91,** 349 (1968).

12. C. S. Carantino, P. D. Wilson, P. Rubin and O. M. Salazar, The optimum radiation schedule in superior vena cava obstruction: importance of ^{99m}Tc scintiangiograms. *Int. J. Radiat. Oncol. Biol. Phys.* **4,** (Suppl. 2), 74 (1978).
13. P. Van Houtte and J. Frühling, Isotopic phlebography in the evaluation of superior vena cava syndrome. *Clin. Nucl. Med.* (In press).