Rapid communication

Levels of neuron-specific enolase after chemotherapy do not predict a response in small cell lung cancer

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Summary. Neuron-specific enolase (NSE) was measured in serum samples of 35 patients with small cell lung cancer and 10 control patients. The samples were collected during 10 days after the first course of chemotherapy, in order to investigate whether changes of NSE had a predictive value for tumour response. Three patterns of change of NSE were observed. Pattern 1 showed an increase of serum NSE with a maximum value more than 1.5 times the pretreatment level (n = 17); pattern 2 involved no increase at all or less than 1.5 times the pretreatment level (n = 14); pattern 3 showed a continuous decrease (n = 5). No relationship between the three patterns of change and the tumour response was observed. Only an NSE level < 10 ng/ml at the time of start of the second course predicted a major response.

Key words: NSE release – Tumour response – Small cell lung cancer

Introduction

Neuron-specific enolase (NSE) is a well-known tumour marker in small cell lung cancer. Raised serum levels were found in 68% of patients with limited disease and 87% of patients with extensive disease (Cooper et al. 1985). Probably NSE is released from dying or dead tumour cells and not actively secreted (Carney et al. 1982). These data seemed to be a logical background from which to investigate whether the change in NSE levels with time after chemotherapy had any predictive value for tumour response, especially in the distinction between a complete remission, partial remission and no remission. In 1982–1983 serum samples were collected from 15 patients for 48–60 h after the start of chemotherapy, but this observation period proved to be too short (unpublished observation). Therefore the study was repeated with a sampling period of 10 days, which is the subject of this paper. In the meantime Akoun et al. (1985), Ariyoshi et al. (1986), and Bork et al. (1988) have reported that a transient elevation of NSE during induction chemotherapy might be an early indicator of tumour response.

Materials and Methods

Patients

Thirty-five patients with small cell lung cancer were staged as having limited or extensive disease by physical examination, chest X-ray, computed tomography scan or ultrasound of the upper abdomen, nuclear bone scan and unilateral bone-marrow biopsy. The patients were treated with chemotherapy according to the EORTC protocol 08825 or 08862 or local protocols. In the EORTC study 08825 patients were treated with 3-weekly courses of cyclophosphamide, adriamycin and Vp16, in the EORTC study 08862 with 4-weekly courses of vincristin and carboplatin or ifosfamide, mesna and carboplatin and in the local protocol with 3-weekly courses of Vp16 and cisplatin. The tumour response was assessed according to WHO criteria (1979) after every two or after five courses. As controls one patient with non-small cell lung cancer and one with small cell lung cancer in complete remission, who received the same chemotherapy as the small cell lung cancer patients, one with melanoma and seven with germ cell tumours, who received cisplatin-based chemotherapy, were used. Serum of all patients was obtained before the start of treatment, every 12 h during the first 2 days and daily during the next 8 days. The samples were stored at −20 °C. Haemolysed samples were not used.

Methods

NSE was measured with the Pharmacia NSE radioimmunoassay test (Pharmacia AB, Uppsala, Sweden) as described previously (Cooper et al. 1985). The NSE values were depicted on semilogarithmic paper.

Results

Serum samples of the 35 small cell lung cancer patients were obtained during 36 courses; samples were col-
selected from one patient both during the first course of chemotherapy and during reinduction chemotherapy at relapse. Thirty-one patients were fully evaluable, two were lost to follow-up and two died early because of toxicity. Thirteen patients had limited disease with a median pretreatment NSE level of 28 ng/ml (range 9.7–132 ng/ml) and 23 had extensive disease with a median pretreatment NSE level of 75 ng/ml (range 10.2–1290 ng/ml). The pretreatment NSE levels in the control patients ranged between 5 and 10 ng/ml.

As shown in Fig. 1 and Table 1 three different patterns of changing NSE levels after chemotherapy were observed. Pattern 1 involved an increase of serum NSE (n=17) with a maximum value more than 1.5 times the pretreatment level at t = 48 h (n = 2), at t = 72 h (n = 2), at t = 96 h (n = 17) and at t >/120 h (n = 6). All late (t >/120 h) maximum levels were observed after carboplatin-based chemotherapy regimes. Pattern 2 showed no increase at all or less than 1.5 times the pretreatment level (n= 14). Pattern 3 showed continuous decrease (n = 5). No relationship between the three patterns of change and tumour response was observed, whereas the percentages of complete, partial or no remission, and limited or extensive disease indicate that the population of patients in this study was not abnormally selected.

In none of the control patients was any increase or decrease of serum NSE observed. All responding patients and none of the non-responding patients had a normal NSE level (below 10 ng/ml) at the start of the second course of chemotherapy, independent of their pretreatment level and type of chemotherapy.

### Discussion

The theoretical background, i.e. a high incidence of elevated NSE levels in small cell lung cancer patients and the presumption that NSE is released from the tumour compartment of dead cells, seemed solid enough.