Eur J Cancer Clin Oncol, Vol. 24, No. 7, pp. 1241–1242, 1988.
Printed in Great Britain

0277-5379/88$3.00+0.00

Letter to the Editor

Serum Insulin-like Growth Factor-I Levels in Patients with Small Cell Lung Cancer

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WE HAVE recently shown that insulin-like growth factor-I (IGF-I)/somatomedin-C is synthesized by small cell lung cancer (SCLC) cell lines and fresh tumour tissue, and is mitogenic to SCLC cells *in vitro* [1]. These findings suggest that IGF-I may function as an autocrine growth factor in SCLC. To determine whether tumour secretion causes measurable elevation of IGF-I levels *in vivo*, we have assayed sera of SCLC patients for IGF-I. The results were assessed with respect to levels of neurone specific enolase (NSE), a known SCLC tumour marker [2].

Between February and December 1987, serum samples were obtained for IGF-I assay on 42 untreated patients with histologically confirmed SCLC. The patients were assessed by means of physical examination, liver function tests (LFTs), chest X-ray, abdominal ultrasound scan and CT brain scan. Patients were staged as having limited disease (LD, tumour confined to one lung and regional lymph nodes) or extensive disease (ED). Acid–ethanol extracted serum samples underwent radioimmunoassay (RIA) for IGF-I, using an anti-IGF-I monoclonal antibody in a competitive assay system modified from a previously described technique [3–5]. Sera were also assayed for NSE using a commercially available RIA kit (Pharmacia Ltd., U.K.).

Accepted 26 February 1988.
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The 42 patients had a median age of 64 years (range 38–77) and included 27 men and 15 women. There were 13 (31%) with limited disease and 29 (69%) with extensive disease. The results of assay for IGF-I and NSE are shown in Table 1. NSE was elevated in 90% of all patients (77% LD, 97% ED). Mean levels were significantly higher in those with ED (98 vs. 19 ng/ml, $P < 0.001$), confirming its correlation with tumour bulk. In contrast there were no IGF-I results above the normal range. Four patients (10%) had levels at or below the lower limit of normal, and there were two (5%) with high/normal values (> 1 u/ml). There was no significant difference between mean levels in the two groups (LD 0.59 ± 0.08, ED 0.53 ± 0.04u/ml).

Serum IGF-I derives mainly from the liver [6], and levels are regulated by nutrition [7]. We therefore related the IGF-I results to liver function and nutritional status. Of the 42 patients, 25 reported steady weight at presentation. Both patients with high/normal levels fell into this group, but the mean level (0.56 ± 0.05 u/ml) was not significantly different from that of 17 patients with a history of anorexia and weight loss (0.52 ± 0.04 u/ml). Twenty-seven patients had normal LFTs and liver appearance on ultrasound scan. Their mean IGF-I value was 0.54 ± 0.04 u/ml. Fifteen patients had hepatic metastases from SCLC, as judged by biochemical and/or scan abnormalities. Their mean level (0.55 ± 0.07 u/ml) was not significantly different from that of the previous group.

In all, serum IGF-I measurements were abnormal in only six of the 42 SCLC patients. Of four

Table 1. Serum IGF-I and NSE levels in 42 patients with SCLC

	IGF-I(u/ml)*			NSE(ng/ml)*		
	Elevated No.(%)	Mean ± S.E.M.	Range	Elevated No.(%)	Mean ± S.E.M.	Range
LD	1 (8)	0.59 ± 0.08	0.15–1.20	10 (77)	19 ± 3	6–38
ED	1 (3)	0.53 ± 0.04	0.14–1.20	28 (97)	98 ± 17	11–400

*Normal levels: IGF-I: 40–60 years 0.32–1.30 u/ml, >60 years 0.20–1.30 u/ml; NSE: <12 ng/ml.

with low levels, two had LD, no history of weight loss and normal LFTs. Low levels in two ED patients may have been related in one to recent weight loss, and in the other to impairment of hepatic function due to liver metastases. Serum IGF-I levels >1 u/ml were recorded in two cases, one with LD and the other ED. The latter had high presenting values of IGF-I (1.20 u/ml) and NSE (33 ng/ml) which fell to normal (0.63 u/ml and 11 ng/ml) with response to chemotherapy. In this patient, the pattern of IGF-I response suggests that we were detecting tumoral IGF-I secretion. However this phenomenon was unusual: serial measurements in six other patients (three LD, three ED) showed chemotherapy-induced fall to normal of the five elevated NSE levels, but no significant change in IGF-I (data not shown).

We conclude that IGF-I levels do not correlate with tumour bulk nor response to therapy in SCLC. Similarly bombesin, another SCLC growth factor [8], had not proved to be a clinically useful tumour marker [9, 10]. These potent peptides are probably secreted in low concentrations by tumour cells, to exert a local (autocrine or paracrine) effect. Thus it may not be surprising that we can rarely detect significant changes in serum levels of tumour growth factors.

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