Growth hormone and malignancy

GS ANDREWS

From the Department of Pathology, Royal Gwent Hospital, Newport, Gwent

SUMMARY The finding of raised growth hormone concentrations in patients with secondary malignancy in the liver is reported. These concentrations were significantly higher than those found in patients with primary malignancy only or in those with non-hepatic secondaries.

A wide range of malignancies was investigated and the high growth hormone concentration was not specific for any type of tumour. This suggested that the increased hormone was not the product of the tumour cells but due to altered liver metabolism.

In 1979¹ we reported raised growth hormone concentrations in six cases of carcinoma of the bronchus with secondary deposits in the liver. A limited investigation of a small number of cases of other carcinomata, at that time, did not reveal any high growth hormone values although a limited rise occurred postoperatively both in some of these carcinoma patients and in patients suffering from non-malignant conditions.

In view of the fact that these findings might have some clinical value, a further study has been carried out to include a wider range of malignancy.

Material and methods

Growth hormone was estimated by radioimmunoassay using the Phadebas hGH Prist Kit. By this method our normal adult basal range is $<1.0-5.0 \mu\text{g/l}$ ($<2.0-10.0 \text{ mU/l}$). This is a double antibody technique, a method which increases the specificity and the second antibody is highly specific for growth hormone. It has been extensively tested and there is no cross reactivity with other human pituitary hormones. There is a well known cross reactivity with human placental lactogen which in a concentration of $16\,000 \mu\text{g/l}$ would alter the growth hormone concentration by $3.5 \mu\text{g/l}$ (7.0 mU/l). This was not relevant to the patients studied.

Serum samples were taken under basal conditions, before 10.00 hrs from a total of 169 cases of malignancy. The carcinoma cases were 74 bronchus, 28 breast, 14 stomach, and 53 others which included carcinoma of the pharynx, larynx, oesophagus, colon, rectum, pancreas, uterus, cervix, ovary, bladder and prostate, and also cases of Hodgkin's disease, malignant melanoma and chronic lymphatic

leukaemia. The numbers in this last group were too few to be considered under individual headings.

Each group was divided into those with primary malignancy only; those with secondaries in the liver, and those with secondaries elsewhere. The presence of secondaries was determined clinically by surgery, radiology, necropsy or biochemical assessment.

Results

These are set out in the Table and all the results are presented in the scatter diagram (Figure). Each group shows a wide scatter and the small number could influence statistical analysis, nevertheless it will be seen that the growth hormone concentration in each type of malignancy and in each subdivision are comparable. The concentrations are higher in the group with liver secondaries and there is also some increase in the group with non-hepatic secondaries. From the Figure it will be seen that the distribution is non-Gaussian and using Hill's method applied to Fisher's exact test there is no statistical difference between the primary tumour groups and those with non-hepatic secondaries ($p = 0.2137$) but there is a highly significant difference both between the primary groups and the liver secondaries groups ($p = 0.000002$) and also between those with liver secondaries and those with secondaries elsewhere ($p = 0.0003$).

Discussion

The high growth hormone concentrations found in patients with secondary carcinoma of the liver are not, as was formerly thought, a specific feature of carcinoma of the bronchus. Ectopic hormone production by non-endocrine tumours has been recognised with increasing frequency. Amongst these car-

Means and standard deviations of growth hormone concentrations ($\mu\text{g/l}$) in the groups studied

Clinical groups	Bronchus			Breast			Stomach			Others		
	No	Growth hormone		No	Growth hormone		No	Growth hormone		No	Growth hormone	
		Mean	SD		Mean	SD		Mean	SD		Mean	SD
Primary carcinoma only	39	1.0	0.92	17	0.88	0.87	8	2.66	3.44	41	1.51	1.41
Secondaries other than in the liver	5	2.16	1.95	6	1.57	1.13	2	2.25	0.49	6	2.63	2.81
Secondaries in liver	30	6.79	7.27	5	9.02	3.89	4	11.77	2.82	6	7.65	7.58

Scatter diagram showing all results

cinoma of the bronchus has figured prominently. The ectopic production of peptide hormones by lung tumours was first described by Liddle *et al*,² Steiner *et al*,³ and Beck and Burger⁴ reported increased growth hormone concentrations in cases of carcinoma of the bronchus, the increased secretion coming from the tumour itself. Similar increases have been reported in cases of carcinoma of the larynx⁵ and some patients with carcinoma of the

prostate have shown an exaggerated growth hormone response to insulin.⁷ Ayalon *et al*⁸ also reported paradoxically high growth hormone concentrations in response to the standard glucose tolerance test in their patients suffering from either carcinoma or atypical hyperplasia of the endometrium. This paradoxical response was abolished after hysterectomy and it was concluded that possibly the abnormal endometrium was producing a growth hormone releasing factor.

In most reported cases attention has been turned to the production of hormones by the tumour cells themselves. Tissue culture has shown that non-endocrine tumour cells are capable of producing a variety of hormones, including growth hormone concentration,⁹ although it has not always been clear that the tumour produced hormone is identical to the natural hormone.

The present findings tend to suggest that the raised growth hormone concentrations could be the result of altered metabolism within the liver, produced by the presence of some tumours. This could be the production of a local substance similar to or closely resembling growth hormone or one which either acts directly on the pituitary or on the hypothalamus.

Despite the wide scatter of values in the liver groups, the finding of raised growth hormone could be of diagnostic value in determining the presence of liver secondaries.

References

¹ Andrews GS. Studies of plasma zinc, copper, caeruloplasmin and growth hormone: with special reference to carcinoma of the bronchus. *J Clin Pathol* 1979;**32**:325-33.
² Liddle GW, Island D, Meador CK. Normal and abnormal regulation of corticotrophin secretion in man. *Recent Progr Horm Res* 1962;**18**:125-66.
³ Steiner H, Dahlback O, Waldenström J. Ectopic growth-hormone production and osteoarthropathy in carcinoma of the bronchus. *Lancet* 1968;**i**:783-5.
⁴ Beck C, Burger HG. Evidence for the presence of immunoreactive growth hormone in the cancers of the lung and stomach. *Cancer* 1972;**30**:75-9.
⁵ Solomon N, Copeland EM, Macfadyan BV Jr, Dudrick SJ, Samaan NA. Intravenous hyperalimentation and growth hormone in cancer patients. *Surg Forum* 1974;**25**:59-60.

Growth hormone and malignancy

- ⁶ Pogosov VS, Shevrygin BV, Shadyr KD. Growth hormone in patients with carcinoma of the larynx. *Vestnik Otorinolaringol* 1976;5:76-7.
- ⁷ Madajewicz S, Bhargava A, Wajzman Z, Mittelman A, Fitzpatrick J, Murphy GP. Hypothalamo-pituitary-adrenal axis in patients with prostatic carcinoma. *Oncology* 1980;37:373-5.
- ⁸ Ayalon D, Peyser MR, Limor R, Lessing JB, Ravid R. Paradoxical hypersecretion of growth hormone in patients with endometrial atypical hyperplasia and carcinoma. Effect of hysterectomy. *Gynecol Obstet Invest* 1982;13:9-16.

Szabo M, Berelowitz M, Pettergill OS, Sorenson GD, Frohman LA. Ectopic production of somatostatin-like immuno- and bioactivity by cultured human pulmonary small cell carcinoma. *J Clin Endocrinol Metab* 1980;51:1048-53.

Requests for reprints to: Dr GS Andrews, Department of Pathology, Royal Gwent Hospital, Newport, Gwent, Wales.

The July 1983 issue

THE JULY 1983 ISSUE CONTAINS THE FOLLOWING PAPERS

Review article

Granulomatous inflammation GT WILLIAMS, W JONES WILLIAMS

Heterogeneity of HLA-DR⁺ cells in normal human kidney. Immunohistological and cytochemical characterisation of discrete cell populations MJ RAFTERY, LW POULTER, G JANOSSY, P SWENY, ON FERNANDO, JF MOORHEAD

Surface membrane staining of immunoglobulins in paraffin sections of non-Hodgkin's lymphomas using immunogold-silver staining technique CS HOLLGATE, P JACKSON, I LAUDER, PN COWEN, CC BIRD

Lectin binding to formalin-fixed paraffin sections A LEATHEM, N ATKINS

Immune complex nephritis in alcoholic cirrhosis: detection of Mallory body antigen in complexes by means of monoclonal antibodies to Mallory bodies J BURNS, AJ D'ARDENNE, JA MORTON, J O'D McGEE

Fibronectin and type III collagen in epithelial neoplasms of gastrointestinal tract and salivary gland AJ D'ARDENNE, J BURNS, BC SYKES, MK BENNETT

Calcium pyrophosphate dihydrate deposition in the intervertebral discs in a case of Wilson's disease J McCLURE, PS SMITH

Liver damage with reversible portal hypertension from vitamin A intoxication: demonstration of Ito cells P GUARASCIO, B PORTMANN, G VISCO, R WILLIAMS

Chronic alcohol excess is associated with selective but reversible injury to type 2B muscle fibres G SLAVIN, F MARTIN, P WARD, J LEVI, T PETERS

Chronic alcoholic skeletal muscle myopathy: a clinical, histological and biochemical assessment of muscle lipid D SUNNASY, SR CAIRNS, F MARTIN, G SLAVIN, TJ PETERS

High-performance liquid chromatographic measurement of amiodarone and desethylamiodarone in

small tissue samples after enzymatic digestion GCA STOREY, PC ADAMS, RWF CAMPBELL, DW HOLT

β cell reserve in cystic fibrosis patients and heterozygotes P DANDONA, ME HODSON, JC BATTEN
Clinical application of a new nephelometric technique to measure complement activation D VERGANI, L BEVIS, BA NASARUDDIN, G MIELI-VERGANI, DEH TEE

Comparison of serum amyloid A protein and C-reactive protein concentrations in cancer and non-malignant disease JG RAYNES, EH COOPER

Plasma spermidine concentrations as early indication of response to therapy in human myeloma OA VAN DOBBENBURGH, B HOUWEN, H JURJENS, J MARRINK, MR HALIE, HO NIEWEG

Effect of ammonium chloride treatment on human polymorphonuclear leucocyte iodination WA PHILLIPS, CS HOSKING, MJ SHELTON

Release of β -thromboglobulin during the preparation, in vitro storage and cryopreservation of platelet concentrates M ANN TAYLOR

Resistance to lysis of erythrocytes containing haemoglobin C—detected in a differential white cell counting system F BOOTH, SUSANNE V MEAD

Comparison of Phadebact coagglutination tests with counterimmunoelectrophoresis for the detection of bacterial antigens in cerebrospinal fluid DS TOMPKINS

Early detection of bacterial growth in blood culture by impedance monitoring with a Bactometer model 32 ANNE BUCKLAND, S KESSOCK-PHILIP, S BASCOMB

A study of the oxygen and carbon dioxide requirements of thermophilic campylobacters FJ BOLTON, D COATES

Letters to the Editor

Book reviews

Some new titles

Notices

Copies are still available and may be obtained from the PUBLISHING MANAGER, BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON WC1H 9JR. Price £5.00, including postage.