Growth hormone and malignancy

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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 1979 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 μg/l (<2.0–10.0 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 μg/l would alter the growth hormone concentration by 3.5 μg/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 = 0.0000002) 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-

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Means and standard deviations of growth hormone concentrations (μg/l) in the groups studied

<table>
<thead>
<tr>
<th>Clinical groups</th>
<th>Bronchus</th>
<th>Breast</th>
<th>Stomach</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Growth hormone</td>
<td>No Growth hormone</td>
<td>No Growth hormone</td>
<td>No Growth hormone</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Primary carcinoma only</td>
<td>39  1.0</td>
<td>0.92</td>
<td>17  0.88</td>
<td>0.87</td>
</tr>
<tr>
<td>Secondaries other than in the liver</td>
<td>5  2.16</td>
<td>1.95</td>
<td>6  1.57</td>
<td>1.13</td>
</tr>
<tr>
<td>Secondaries in liver</td>
<td>30  6.79</td>
<td>7.27</td>
<td>5  9.02</td>
<td>3.89</td>
</tr>
</tbody>
</table>

Scatter diagram showing all results

Carcinoma of the bronchus has figured prominently. The ectopic production of peptide hormones by lung tumours was first described by Liddle et al., Steiner et al., and Beck and Burger 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 larynx and some patients with carcinoma of the prostate have shown an exaggerated growth hormone response to insulin. Ayalon et al. 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, 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

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