Spontaneous hypoglycaemia and pleural fibroma: role of insulin like growth factors

N E Moat, J D Teale, R E Lea, A W Matthews

Abstract
Spontaneous hypoglycaemia was the presenting feature of a man with a large subpleural fibroma. Preoperative and postoperative studies support the view that the tumour induced hypoglycaemia was due to the secretion of peptide hormones by the tumour.

It has long been recognised that tumours other than those of pancreatic islet cells may present with spontaneous hypoglycaemia. They are usually large mesenchymal tumours and include pleural fibromas. Of the numerous hypotheses explaining this phenomenon, the most plausible is that the tumour secretes substances with insulin-like activity.

Case report
A 57 year old non-smoker with no relevant medical history presented with two episodes of confusion, unusual behaviour, and sweating that were relieved by food. On examination he had finger clubbing and there was dullness to percussion with reduced breath sounds over the left upper chest. A chest radiograph and computed tomogram showed a large rounded mass occupying the upper half of the left hemithorax. Percutaneous needle biopsy showed a spindle cell tumour, suggesting a subpleural fibroma. His fasting blood glucose concentration was 2.1 mmol/l. Plasma insulin, C peptide, and growth hormone concentrations were also low given the presence of hypoglycaemia (table). Further investigations showed that the plasma concentration of insulin like growth factor I (IGF I) was abnormally low when compared with relevant reference values, whereas that of IGF II was normal; thus the IGF I : IGF II ratio was considerably reduced (table).

At operation a large tumour was found, arising from the parietal pleura at the left apex, compressing but not invading the lung. The tumour was completely excised and macroscopically was an encapsulated, lobulated mass measuring 16 × 10 × 16 cm. Histological examination showed fibroblastic proliferation with regions of increased cellularity typical of a subpleural fibroma. The mitotic rate was high for this type of tumour.

The patient made an uneventful recovery and had no further hypoglycaemic episodes. The biochemical studies were repeated six months later and fasting blood glucose, insulin, and growth hormone concentrations were in the normal range. The concentration of IGF I and the IGF I : IGF II ratio had returned to the normal range (table).

Discussion
Tumour induced hypoglycaemia was first described by Doee in 1930. A large variety of tumours have been implicated, particularly those involving fibrous proliferations. In a review of 368 cases of pleural fibroma there was a 4% incidence of spontaneous hypoglycaemia; this was more likely to occur with larger tumours and those with a high mitotic rate. Non-islet cell tumours may secrete peptides with insulin like activity. The insulin like growth factors (I and II) are polypeptides with a weak insulin like effect. Unlike most peptide hormones they are bound strongly to specific binding proteins in blood. The production of both insulin like growth factors and their main binding protein is usually controlled by growth hormone. Insulin like growth factors suppress growth hormone secretion by negative feedback. The published evidence concerning their concentrations in patients with tumour associated hypoglycaemia is contradictory. These discrepancies may be explained by methodological differences and difficulties in assaying these peptides.

Further evidence in favour of the production of insulin like growth factors are the high concentrations of messenger RNA for IGF II in excised mesenchymal tumours. Autonomic secretion of insulin like growth factor II by such tumours may lead to suppression of plasma growth hormone concentrations and

Biochemical data immediately before and six months after surgical excision of a pleural fibroma

<table>
<thead>
<tr>
<th>Reference value</th>
<th>Glucose (mmol/l)</th>
<th>Growth hormone (mU/l)</th>
<th>IGF I (U/ml)</th>
<th>IGF II (U/ml)</th>
<th>IGF I : IGF II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>2.1</td>
<td>2.9</td>
<td>0.3-1.2</td>
<td>0.4-1.3</td>
<td>&gt; 0.21</td>
</tr>
<tr>
<td>Postoperative</td>
<td>5.2</td>
<td>14.7</td>
<td>1.24</td>
<td>0.96</td>
<td>1.29</td>
</tr>
</tbody>
</table>

IGF—insulin like growth factor.
*Insulin and C peptide were detectable postoperatively but not preoperatively.
1During hypoglycaemia.
2See Teale and Marks.
Endoscopic bougie and balloon dilatation of multiple bronchial stenoses: 10 year follow up

J B Ball, J C Delaney, C C Evans,
R J Donnelly, C R K Hind

Abstract
This paper reports 10 year follow up data on four patients who underwent mechanical dilatation of multiple bronchial stenoses (sarcoidosis two cases, berylliosis one case, idiopathic stenoses one case). Two patients enjoyed symptomatic and physiological improvement during the nine years before they presented with a recurrence of stenosis. The other two had recurrences sooner, and improved only slightly after they had started prednisolone treatment.

In 1981 the Liverpool Cardiothoracic Centre reported four cases in which bougie dilatation at rigid bronchoscopy was used successfully to treat multiple bronchial stenoses. Ten years later we have reviewed the outcome. Two of the patients have biopsy proved sarcoidosis, one idiopathic bronchostenoses, and one berylliosis.

Case reports
CASE 1
A 51 year old man was diagnosed as having pulmonary sarcoidosis in 1971 by endobronchial biopsy. During 1973–8 he developed progressive exertional dyspnoea and had recurrent chest infections. He presented in 1979 with breathlessness on mild exertion, stridor, fixed wheeze in the left midzone, and reduced breath sounds at both apices. The flow-volume loop suggested central airway obstruction and tomography showed bilateral bronchial stenoses.
Fibreoptic bronchoscopy showed multiple fibrotic stenoses with pale, non-erythematous mucosa. The segmental bronchi of the right upper lobe were narrowed to 0.5–2.0 mm and the right middle lobe bronchi to 3.0 mm. In the left lung the diameters of the orifices of the upper lobe, lingula, and lower lobe bronchi...
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