A Novel Cause of Hypoglycaemia Secondary to Non-Islet Cell Tumour

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Introduction

Hypoglycaemia is uncommon in adults who are not being treated for diabetes and may be due to varied aetiologies. The mechanism in non-diabetic hypoglycaemia may result from excessive insulin or insulin-like activity (IGF-2), reduced gluconeogenesis, disruption of hepatic glucagon metabolism, or increased glucose utilisation.

From an endocrinology perspective, causes of interest include endogenous hyperinsulinaemia (insulinoma, non-insulinoma pancreatogenous hypoglycaemia and autoimmune hypoglycaemia) and non-islet cell tumours.

This case demonstrates a novel cause of hypoglycaemia secondary to ectopic insulin secretion in association with a mixed disseminated high grade neuroendocrine carcinoma of the prostate.

Investigation

- The suspicious examination finding was investigated with CT scan of thorax, abdomen and pelvis in which disseminated malignancy involving the liver, lungs and spine with no primary tumour identified.
- A significantly elevated PSA pointed towards prostate cancer as the likely primary and the elevated CA-19-9 was attributed to the hepatic metastasis (Table 1). An elevated chromogranin A suggested a neuroendocrine element which complicated the interpretation.
- PET scan confirmed multiple bone metastasis involving the femurs and humerus. Liver biopsy was obtained in attempt to identify the primary tumour and define management plans.
- Capillary blood glucose of 1.9 mmol/L was obtained following three hours of monitored fasting with concurrent serum sample showed in table 2.

Case Report

Seventy three year old male presenting with new onset of recurrent episodic symptoms consistent with hypoglycaemia (slurring of speech, sweating, agitation and confusion) and pre-hospital capillary glucose less than 1 mmol/L with resolution of symptoms after treatment with oral glucose.

The past medical history was unremarkable and no precipitating factors were found.

The finding on clinical examination was hepatomegaly with irregular edge.

Recurrent hypoglycaemia was initially avoided by high oral glucose intake with intensive blood glucose monitoring, however this was insufficient to prevent nocturnal hypoglycaemic episodes.

Initial Management

- Prednisolone was started to mitigate overnight hypoglycaemia which initially controlled blood glucose levels.
- As rapid recurrent hypoglycaemia ensued, continuous IV infusion of 10% dextrose was initiated with the following treatments:
  - Diazoxide (orally)
  - Octreotide (subcutaneously)
  - Degarelix (GnRH antagonist) was commenced for presumed advanced prostate adenocarcinoma
- In respect of patient’s wishes, active treatment was withdrawn with comfort being made the priority.

Outcome

- The liver biopsy showed high grade neuroendocrine carcinoma without an obvious primary origin with negative immunohistochemistry testing for prostate specific antigen and insulin.
- Post-mortem examination revealed a large infiltrated prostate containing both adenocarcinoma (poor and well differentiated) and high grade neuroendocrine (small and non-small cell) carcinoma with extensive metastasis of the neuroendocrine carcinoma and normal pancreas and gastrointestinal tract.
- This to our knowledge is the first report of ectopic insulin secretion in association with a mixed disseminated high grade neuroendocrine carcinoma of the prostate.

Table 1: Tumour markers

<table>
<thead>
<tr>
<th>Tumour Marker</th>
<th>Result</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSA</td>
<td>62.7 ug/L</td>
<td>0.1-6.5</td>
</tr>
<tr>
<td>CA-19-9</td>
<td>308 KU/L</td>
<td>0-35</td>
</tr>
<tr>
<td>CEA</td>
<td>2.5 ug/L</td>
<td>0-2.5</td>
</tr>
<tr>
<td>AFP</td>
<td>3KU/L</td>
<td>0-20</td>
</tr>
<tr>
<td>Chromogranin A</td>
<td>16.5 mmol/L</td>
<td>0-6</td>
</tr>
</tbody>
</table>

Table 2: Serum levels with capillary glucose 1.9 mmol/L

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Glucose</td>
<td>&lt;0.1 mmol/L</td>
<td>17.8-173</td>
</tr>
<tr>
<td>Insulin</td>
<td>224.3 pmol/L</td>
<td>298-3350</td>
</tr>
<tr>
<td>C-Peptide</td>
<td>1953 pmol/L</td>
<td>47-207</td>
</tr>
<tr>
<td>IGF-1</td>
<td>25ug/L</td>
<td>0.5-3.1</td>
</tr>
<tr>
<td>IgG Insulin autoantibodies</td>
<td>3.1 mg/L</td>
<td>0.5-2.0</td>
</tr>
</tbody>
</table>

References
4. BES2017 Neoplasia, cancer and late effects

Poster presented at: Sheffield Research Centre, United Kingdom