Isolated ACTH deficiency accompanied by ‘primary hypothyroidism’ and hyperprolactinaemia

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Abstract. A 55 year old man with isolated ACTH deficiency is reported. The lesion would appear to be located in the pituitary gland since plasma ACTH and cortisol did not respond to lysine vasopressin and corticotrophin releasing factor (CRF). A fall in T₄, a rise in basal values of TSH, prolactin (Prl), LH and FSH, excessive responses of TSH and Prl to TRH, and hyperreactive responses of LH and FSH to LRH were observed. These hormonal changes were examined before and after administration of cortisol. The abnormality in these hormones might be caused by deficiency of long-term glucocorticoid.

Isolated ACTH deficiency (Steinberg et al. 1954; Stacpoole et al. 1982) is rare but variable in its manifestations. Some patients present with anorexia, vomiting, fever and emaciation and others with neuropsychiatric symptoms. In this study to determine whether a primary lesion lay in the pituitary gland or the hypothalamus tests using hypoglycaemia, lysine vasopressin and CRF were performed. Hormonal changes before and after administration of cortisol were studied in this case, and a fall in T₄, elevated basal values for TSH and Prl and hyperreactive responses to TRH and LRH were demonstrated.

Case Report

A 55 year old man was admitted with the complaints of anorexia, emaciation and disturbance of gait. At the beginning of January, 1982, he noticed fatigability. In February of the same year, his appetite diminished and nausea and vomiting occurred occasionally and his weight decreased; slight fever and night sweats were also noted. Early in March, he had difficulty in standing and a disturbance of gait appeared. On April 17, he was admitted to hospital and investigations included serum biochemistry, CT scan of the head, lumbar puncture and electroencephalography. He was discharged with no abnormality found. From the middle of May, pain in the left elbow joint and morning stiffness of the fingers began to appear. On July 2, he was admitted for an intensive check-up.

Physical examination on admission: emaciation was conspicuous. The level of consciousness was normal but he appeared apathetic and pallid. The skin was dry and coarse, and turgor was decreased markedly. His blood pressure was 88/58 mmHg; pulse 68/min and regular. Vision and visual fields were normal. Ocular movement was normal. The mouth was normal. There was no enlargement of lymph nodes or thyroid. Gynaeomastia was observed. The chest and abdomen were not remarkable, and there was no oedema. Axillary and pubic hair was present. He was unable to stand on tiptoe or on his heels. There was no paralysis in the upper and lower extremities, but the muscle was lean with decreased muscular strength. Tendon reflexes were normal. There were no pathological reflexes. There was no sensory disturbance. The function of cerebellum was normal.

Urinalysis and stool examination were normal. Examination of peripheral blood disclosed mild hypocromic and microcytic anaemia with moderate eosinophilia and lymphocytosis. All routine laboratory examinations, including serum enzymes and electrolytes (Na 139 and K 4.5 mEq/l), were normal. The fasting blood sugar was 65 mg/dl. Total cholesterol was 130 mg/dl. The thyroid...
test and microsone test were 100-fold or less. X-ray films of the head showed no abnormality in the skull and sella turcica. EEG was a low voltage on the whole but showed no asymmetry or spike waves.

Tables 1 and 2 show the results of the endocrine examination.

On the basis of the clinical course, symptoms and laboratory data described above, this case was diagnosed as isolated ACTH deficiency accompanied by 'primary hypothyroidism' and hyperprolactinaemia.

Clinical course: cortisol (25 mg/day) was administered. Improvement in mental function and appetite as well as weight gain and a rise in the blood pressure were noticed after administration. Pain in the breast also subsided.

Results of the hormone assay after medication are shown in Table 3. T₄ was normalized; the basal value of TSH was high and excessively responsive to TRH. Prl was also normalized and showed an excessive response to TRH.

Discussion

Isolated ACTH deficiency was reported by Steinberg et al. (1954) for the first time. With the progress of endocrinology, the cases reported have since increased in number, but 50–60 cases are all that have been reported up to the present. Clinical symptoms often reported in this disease – anorexia, nausea, vomiting, weight loss, fever, general fatigue and fatigability – were observed in our case too. These symptoms are said to be variable, non-specific and similar to the symptoms and signs of adrenocortical insufficiency (Stacpoole et al. 1982). Investigations have reportedly revealed abnormalities such as hypotension (26%), hypoglycaemia (56%), anaemia (26%), hyponatraemia (9%), hypercholesterolaemia, eosinophilia and lymphocytosis (Stacpoole et al. 1982). These findings are also variable and non-specific. All of these features apart from hyponatraemia were present in this case.

The pituitary body or hypothalamus is suspected to be the site of the lesion in this disease. It is said that CRF and lysine vasopressin act directly on the pituitary body for secretion of ACTH and that hypoglycaemia acts on the pituitary gland through the hypothalamus for secretion of ACTH (Stacpoole et al. 1982; Staub et al. 1973). In our case,
### Table 2.
Results of various hormone estimations.

1. **ACTH stimulation test (ACTH 1 mg im for 4 days)**

<table>
<thead>
<tr>
<th></th>
<th>Basal</th>
<th>1st day</th>
<th>2nd day</th>
<th>3rd day</th>
<th>4th day</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH (pg/ml)</td>
<td>15</td>
<td>50</td>
<td>62</td>
<td>108</td>
<td>53</td>
</tr>
<tr>
<td>Cortisol (µg/dl)</td>
<td>1.0</td>
<td>26.6</td>
<td>43.4</td>
<td>43.2</td>
<td>52.8</td>
</tr>
<tr>
<td>17-OHCS (mg/day)</td>
<td>0.3</td>
<td>3.7</td>
<td>17.7</td>
<td>28.2</td>
<td>35.1</td>
</tr>
</tbody>
</table>

2. **Metyrapone test (0.5 g qid for 1 day)**

<table>
<thead>
<tr>
<th></th>
<th>Basal</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH (pg/day)</td>
<td>23</td>
<td>25</td>
</tr>
<tr>
<td>17-OHCS (mg/day)</td>
<td>0.3</td>
<td>0.6</td>
</tr>
<tr>
<td>17-KS (mg/day)</td>
<td>1.4</td>
<td>1.3</td>
</tr>
</tbody>
</table>

3. **Lysine vasopressin test (10 U im)**

<table>
<thead>
<tr>
<th></th>
<th>Basal</th>
<th>15</th>
<th>30</th>
<th>45</th>
<th>60</th>
<th>75</th>
<th>90</th>
<th>120 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH (pg/ml)</td>
<td>48</td>
<td>54</td>
<td>54</td>
<td>62</td>
<td>50</td>
<td>10</td>
<td>47</td>
<td>45</td>
</tr>
</tbody>
</table>

4. **CRF test (45 U iv)**

<table>
<thead>
<tr>
<th></th>
<th>Basal</th>
<th>5</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>60</th>
<th>90</th>
<th>120 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH (pg/ml)</td>
<td>24</td>
<td>10</td>
<td>26</td>
<td>14</td>
<td>22</td>
<td>13</td>
<td>15</td>
<td>25</td>
</tr>
</tbody>
</table>

5. **Triple test**
(regular insulin 0.05 U/kg, TRH 500 µg and LRH 100 µg iv)

<table>
<thead>
<tr>
<th></th>
<th>Basal</th>
<th>30</th>
<th>60</th>
<th>90</th>
<th>120 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum glucose (mg/dl)</td>
<td>68</td>
<td>28</td>
<td>138</td>
<td>42</td>
<td>111</td>
</tr>
<tr>
<td>ACTH (pg/dl)</td>
<td>39</td>
<td>43</td>
<td>36</td>
<td>54</td>
<td>62</td>
</tr>
<tr>
<td>Cortisol (µg/dl)</td>
<td>1.5</td>
<td>1.9</td>
<td>1.8</td>
<td>2.2</td>
<td>2.4</td>
</tr>
<tr>
<td>GH (ng/ml)</td>
<td>2.7</td>
<td>14.8</td>
<td>21.6</td>
<td>20.6</td>
<td>16.8</td>
</tr>
<tr>
<td>TSH (µU/ml)</td>
<td>26.2</td>
<td>66.3</td>
<td>65.4</td>
<td>58.2</td>
<td>48.4</td>
</tr>
<tr>
<td>Prl (ng/ml)</td>
<td>25.4</td>
<td>165.1</td>
<td>120.6</td>
<td>93.3</td>
<td>69.9</td>
</tr>
<tr>
<td>LH (mIU/ml)</td>
<td>25.7</td>
<td>141.7</td>
<td>111.3</td>
<td>104.4</td>
<td>95.9</td>
</tr>
<tr>
<td>FSH (mIU/ml)</td>
<td>18.7</td>
<td>24.1</td>
<td>25.6</td>
<td>25.8</td>
<td>26.6</td>
</tr>
</tbody>
</table>

Hypoglycaemia occurred during the test. Glucose was administrated iv.
ACTH was not secreted with hypoglycaemia, CRF or lysine vasopressin, leading us to suspect a lesion in the pituitary gland. However, if CRF is deficient over a long period, the ACTH secreting cell may become atrophied and so will not respond to a single injection of CRF. This possibility cannot be ruled out. The truth of the claim that a hypothalamic lesion can be differentiated from a pituitary one by the lysine vasopressin test will have to be confirmed by continuous infusion of CRF and lysine vasopressin.

Diagnostic criteria mentioned in this disease include 1) low values for urine 17-OHCS, 2) plasma ACTH is decreased or normal, 3) an increase in plasma cortisol and 17-OHCS after continuous administration of ACTH (Topliss et al. 1980), no rise in 17-OHCS after administration of metyrapone (Barnett et al. 1982) and no decrease in secretion of other pituitary hormones (Stacpoole et al. 1982). However, cases with high values for TSH and Prl have been reported (Topliss et al. 1980; Barnett et al. 1982). A low T₄, high values for TSH and an excessive response of TSH to TRH suggested that primary hypothyroidism was a complication in our case.

In our case, high values of TSH and an excessive response of TSH were still found but T₄ was normalized in testing performed 2 weeks after administration of cortisol, showing that cortisol exerted an influence on thyroid function. Clinically, findings suggestive of hypothyroidism were not observed. So, this case was considered not as primary hypothyroidism but as a case in which apparent hypothyroidism had developed secondary to adrenal insufficiency. It has been shown that TSH rises over a long period of glucocorticoid deficiency and high values of TSH cannot serve as an index of thyroid function in adrenal insufficiency (Topliss et al. 1980; Barnett et al. 1982).

In our case the basal value for Prl was also high and Prl showed an excessive response to TRH: Prl fell slightly 2 weeks after administration but still showed an excessive response to TRH. It has been reported that glucocorticoid inhibits Prl secretion partially in man (Copinschi et al. 1975) and that dexamethasone does not inhibit Prl secretion (Re et al. 1976). High Prl values in this disease may be attributable to cortisol deficiency.

References


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