PREGNANCY INDUCED CUSHING’S SYNDROME

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INTRODUCTION

Misdiagnosis of Cushing syndrome (CS) is common because of the overlapping features of fatigue, weight gain, striae and emotional changes that occur during normal pregnancy.

The clinical presentation together with laboratory and imaging findings help to make a diagnosis. However, changes in maternal hormones and their binding proteins complicate assessment of the normal level of glucocorticoid hormones during gestation.

CS during pregnancy is attributable most frequently to an adrenal adenoma and to a lesser degree to adrenocorticotrophic hormone hypersecretion from a pituitary adenoma. Furthermore aberrant expression of various hormone receptors in the adrenal glands have been suggested to be involved in the pathogenesis of this condition, in particular the luteinizing hormone receptor.

METHODS

We investigated and treated three pregnant women with ACTH-independent Cushing's syndrome and an adrenal tumor.

After uncomplicated delivery patient 1 underwent in vivo testing for aberrant hormone receptor expression by the adenoma.

Adrenal tumor tissue of patient 1 and 2 were stained immunohistochemical for LH receptors.

RESULTS

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diurnal cortisol rhythm (nmol/l)</th>
<th>Salivary cortisol (nmol/l)</th>
<th>UFC (nmol/24h)</th>
<th>1 Mg-DST (nmol/l)</th>
<th>ACTH (pmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>During pregnancy</td>
<td>690 - 1070 - 1030</td>
<td>Not measured</td>
<td>1380</td>
<td>360</td>
<td>&lt; 1.1</td>
</tr>
<tr>
<td>After delivery</td>
<td>320 - 596 - 280</td>
<td>18 - 12 - 47 - 64</td>
<td>582</td>
<td>210</td>
<td>&lt; 1.1</td>
</tr>
</tbody>
</table>

Cortisol response was found after administration of:
- LHRH (211%) en hCG (155%),
- ACTH (213%),
- TRH (133%),
- Standard mixed meal (392% and 140%),
- Glucagon (347%),
- Vasopressine (198%).

CONCLUSIONS

Considering the cortisol responses to LHRH and hCG, and the development of CS during pregnancy in these patients, it is likely that ACTH-independent hypercortisolism was induced by the pregnancy-associated rise in hCG levels that activated aberrantly expressed LH receptors in the adrenal adenoma.

Remarkably adrenal adenomas may simultaneously express multiple aberrant receptors and individual ligands may play a role in the regulation of cortisol production responsible for pregnancy induced CS.

REFERENCES

Feelders et al., JCEM, 88(1):230-237
Lacroix, et al., Endocrine Review, 22(1):75-110
Lindsay et al., JCEM, 90(5):3077-3083
Mazzuco et al., JCEM, 91(1):196-203