Food Refusal, Loss of Appetite, Chronic Fatigue and Depression due to Central Adrenal Insufficiency Presenting as Anorexia Nervosa in an Adolescent Girl

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Abstract

The hypothalamic-pineal region is involved in the regulation of different functions in our body like the regulation of hunger, thirst, temperature and reproduction. In one 14-year-old anorexia nervosa patient we found low levels of ghrelin in the acute stage and during the whole refeeding procedure, suggestive of an underlying endocrine problem. The refeeding process in our patient was difficult. An insulin stimulation test was done and we observed no response of ACTH and cortisol secretion to severe hypoglycemia. Central adrenal insufficiency was found and supplementation with hydrocortisone was started. Central adrenal insufficiency explained also the difficulties in the water and sodium balance following ingestion of DDAVP for enuresis nocturna and carbamazepine for an epileptic insult.

Keywords: Anorexia nervosa; Food refusal; Chronic fatigue syndrome; Depression; Central adrenal insufficiency

Introduction

The estimated prevalence of secondary and tertiary (central) adrenal insufficiency is 150-280 per million [1]. A lot of processes that involves the hypothalamus and which interferes with Corticotrophin-Releasing Hormone (CRH) secretion like hypothalamic tumors, surgery, irradiation and autoimmune hypothalamic disease will result in central adrenal failure [2]. The symptoms that we encounter in these patients are weakness, fatigue, myalgias and psychiatric symptoms and are misdiagnosed as depression and as chronic anxiety disorders [3].

Case Report

A 14-year-old girl with a restrictive type of anorexia nervosa since the age of 13 years (BMI: 12.2 kg/m2) was admitted to our tertiary eating disorder department. Her personal history was complicated by a hemolytic-uremic syndrome at the age of 4.5 years. After recovery of this nephrologic insult, she suffered from persistent enuresis nocturna, resistant to different treatments. At the age of 10 years old she developed an epileptic insult and was treated with carbamazepine. At the age of 12 years she received for her still persistent enuresis nocturna a treatment with DDAVP. During that treatment she developed chronic sodium deficiency, macrocytic anemia and weight loss. The family history was notable for several episodes of depression in her mother, who took multiple medications to brake her appetite. At the time of presentation patient's oral temperature was 35.9°C, blood pressure 75/46 mm Hg taken in sitting position with an electronic device, pulse rate was 45 bpm, oxygen saturation was 99% in room air. Her weight was 26.4 kg, height: 147 cm and BMI: 12.2 kg/m². On examination her heart sounds were regular but bradycardic and there were no abnormal lung sounds. Abdominal examination was normal. She had split back and face; the extremities were acrocyanotic with livido reticularis from feet to knees. The capillary refill was delayed and there was no pitting edema. Cardiac and electrocardiographic measurements in the acute stage: QTc dispersion: 48 msec; QT interval: 387 msec; QTc interval: 368 msec; LVM: 64.34 g; LVM: height2.7: 25.57 g/m2.7. The refeeding process in our patient was difficult. An insulin stimulation test was done and we observed no response of ACTH and cortisol secretion to severe hypoglycemia (Table 1). Central adrenal insufficiency was found and supplementation with hydrocortisone was started. Afterwards her symptoms ameliorated and disappeared after nearly one year.

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Discussion

Adrenal insufficiency is a life-threatening condition that may result from primary adrenal failure or from impairment of the hypothalamic-pituitary adrenal (HPA) axis [1-4]. Patients with central adrenal insufficiency are a diagnostic challenge [5]. The reference tests for establishing the integrity of the HPA axis rely on a response to either a strong stimulus [e.g. insulin-induced hypoglycemia/insulin tolerance test (ITT)], or the interruption of negative feedback (overnight metyrapone test). The ITT is contraindicated in infants and children with a history of seizures or cardiovascular disease and requires continuous monitoring [6].

Central adrenal insufficiency explained also the difficulties in the water and sodium balance following ingestion of DDAVP for enuresis nocturna and carbamazepine for an epileptic insult in our patient.

The reported incidence of carbamazepine-induced hyponatremia varies between 4.8 to 40%. Carbamazepine has been associated with the Syndrome of Inappropriate Antidiuretic Hormone (SIADH) secretion, due to an impaired sensitivity of hypothalamic osmoreceptors to serum osmolality and an increased renal sensitivity of the renal tubules to circulating vasopressin [7,8]. Carbamazepine dose and plasma levels are probably related to the risk of hyponatremia, while the duration of the treatment does not contribute to the hyponatremia [7-9].

Desmopressin (DDAVP) used for enuresis nocturna in our patient causes hyponatremia in 15% of the pediatric population. Factors that predispose to hyponatremia are a higher dose, higher age (>65 years of age), a low-normal serum sodium, a high 24-hour urine volume and co-medication (thiazides, tricyclic antidepressants, serotonin-reuptake-inhibitors, chlorpromazine, carbamazepine, loperamide, non-steroidal-anti-inflammatory-drugs [4-10].

Table 1: Insulin test: no excretion of ACTH and cortisol on severe hypoglycemia.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Glycemia (mg/dl)</th>
<th>ACTH (pg/ml)</th>
<th>Cortisol (µg/dl)</th>
<th>GH (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>80</td>
<td>13</td>
<td>5.56</td>
<td>1.07</td>
</tr>
<tr>
<td>20</td>
<td>25</td>
<td>13</td>
<td>3.70</td>
<td>0.73</td>
</tr>
</tbody>
</table>

Table 1: Insulin test: no excretion of ACTH and cortisol on severe hypoglycemia.

Conclusion

Tertiary adrenal insufficiency is due to a hypothalamic disease and decrease in Corticotropin Releasing Factor (CRF). Oxidative damage to any of the HPA-Axis organs can be the cause of “Chronic Fatigue Syndrome” with difficulties of refeeding in our patient. Therefore in these patients with anorexia with refeeding difficulties, no hunger sensation and with chronic fatigue syndrome a central adrenal insufficiency must be excluded.

References