Isolated Adrenocorticotropic Hormone Deficiency (ACTH) Associated with Hashimoto’s Disease

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Abstract

Isolated adrenocorticotropic hormone (ACTH) deficiency (IAD) is a rare disease characterized by secondary adrenal insufficiency with low cortisol production and normal secretion of pituitary hormones other than ACTH. Association of IAD with Hashimoto’s disease (HD) is rare. This suggests the possibility of common autoimmune process affecting both the pituitary and the thyroid glands. Here, we report two cases of IAD with HD.

Key words: Adrenocorticotropic hormone (ACTH), hashimoto’s disease

Introduction

Isolated adrenocorticotropic hormone (ACTH) deficiency (IAD) is a rare disease characterized by secondary adrenal insufficiency with low cortisol production and normal secretion of pituitary hormones other than ACTH (1). Association of IAD with Hashimoto’s disease (HD), which is characterized by autoimmune origin, is rare. This suggests the possibility of common autoimmune process affecting both the pituitary and the thyroid glands.

Here, we report two cases of IAD with HD in two patients who presented with anorexia, nausea, vomiting, and weight loss.

Case Reports

Patient 1

A 84-year-old man presented with anorexia, nausea, vomiting, and an unintentional weight loss of 13 kg in the past 3 months. His physical examination was normal. Endoscopy revealed a Mallory-Weiss tear in the esophagus, thus, sclerotherapy was performed. Colonoscopy was unremarkable. Blood tests revealed a low level of sodium (129 mEq/l) and a potassium level within the normal range. Laboratory tests showed hypothyroidism with plasma levels of free T3 of 1.89 pg/ml (1.17–3.71), free T4 of 0.47 ng/ml (0.7–1.48) and high TSH of 19.2 mIU/ml (0.35–1.94). The autoimmune antibodies were positive (anti-TPO: 538 IU/ml (0–35), anti-TG: 537 IU/ml (0–40)) and the cortisol level was found to be 1.22 mcg/dl. Adrenal insufficiency was considered because of the presenting symptoms (sodium was low at 120 mEq/l with normal potassium and cortisol was found to be 1.22 mcg/dl). Measurement of ACTH level was done for differential diagnosis between primary and secondary adrenocortical insufficiency, ACTH levels were determined as 3.4 pg/ml. The patient was diagnosed with secondary adrenocortical insufficiency. Due to advanced age, we did not perform insulin tolerance test (ITT) to confirm the diagnosis. The levels of other pituitary hormones were within normal limits. Dehydroepiandrosterone sulfate (DHEA-S) was declined (18.7 μg/dl (80–560 μg/dl)). Levels of the other pituitary hormones were as follows: FSH: 4.04 mIU/ml (1.38–13.58), LH: 5.22 mIU/ml (1.7–8.6), prolactin: 15.96 ng/ml (2.58–18.12), GH: 0.18 ng/ml, total testosterone: 6.39 ng/ml (1.56–5.63), progesterone: 0.1 ng/ml (0.2–1.4), DHEA-S of 18.7 ug/dl (80–560).
Pituitary magnetic resonance imaging was normal. Hydrocortisone and L-thyroxine treatment was administered to the patient who received the diagnosis of IAD and hypothyroidism. The clinical and electrolyte abnormalities improved after the treatment.

**Patient 2**

A 45 year-old man presented with anorexia, nausea, vomiting. He had the complaint of fatigue for the past 3-4 years. His physical examination was normal. The patient had hypothyroidism but he did not receive any treatment for the past 2 years. The diagnosis of hypothyroidism was confirmed based on the laboratory tests which revealed plasma levels of free T3 of 2.41 pg/ml (1.71-3.71), free T4 of 0.46 ng/ml (0.7-1.48) and TSH of 47.67 mIU/ml (0.35-1.94). The autoimmune antibodies were positive (anti-TPO: 233 IU/ml (0-35), anti-TG: 309.2 IU/ml (0-40)) and cortisol level was found to be 0.29 mcg/dl.

Measurement of ACTH was performed for differential diagnosis between primary and secondary adrenocortical insufficiency. The ACTH level was determined to be 5.59 pg/ml. The patient was diagnosed with secondary adrenocortical insufficiency. The levels of the other pituitary hormones were as follows: FSH: 3.26 mIU/ml (1.38-13.58), LH: 13.09 mIU/ml (1.7-8.6), prolactin: 40.35 ng/ml (2.58-18.12), GH: 0.05 ng/ml, total testosterone: 6.74 ng/ml (1.56-5.63).

Insulin-induced hypoglycemia test was performed. When the patient’s blood glucose was 38 mg/dl, the cortisol level was measured as 0.41 ug/dl. Cortisol responce was insufficient. Pituitary magnetic resonance imaging was normal. The patient, who received the diagnosis of IAD and hypothyroidism, was treated with hydrocortisone and L-thyroxine.

**Discussion**

ACTH deficiency is generally associated with diminished growth hormone (GH), gonadotropin or TSH reserve with the partial or total pituitary insufficiency [2]. IAD is characterized by secondary adrenal insufficiency with low or absent cortisol production and normal secretion of pituitary hormones other than ACTH. IAD accounts for only a small part of secondary adrenal insufficiency. The etiology of IAD is still unknown but an autoimmune mechanism was accused of in some cases. In a study on 176 patients with secondary adrenal failure, it was reported that 63% of patients had a co-existing autoimmune disease, such as primary hypothyroidism, primary hyperthyroidism, vitiligo, type 1 DM, and pernicious anemia; besides, thyroid autoantibodies were positive in 60% of subjects. The authors reported the possibility of the presence of an autoimmune process in IAD due to the high incidence of autoimmune disorders in patients with secondary adrenal failure [3]. However, in this large series, which reported a high prevalence of autoimmune diseases in patient with IAD, any specific antibodies or factors causing the loss of ACTH function were not detected [3]. Our results are compatible with those of this study.

IAD is a rare disorder with variable clinical presentations [4]. Patient with IAD present with non-specific symptoms, such as asthenia, anorexia, unintentional weight loss, or tendency to hypoglycemia (2). Therefore, to establish the diagnosis is often challenging. However, with the early diagnosis and treatment, all symptoms may improve. Digestive problems are the most common symptoms in patients with adrenal insufficiency, however, the diagnosis of adrenal insufficiency in such patients is difficult (5). In the literature, the case of IAD in a patient who presented with recurrent oesophageal ulceration resulting in oesophageal stenosis has been reported. The recurrent oesophageal ulcers were due to digestive symptoms of adrenal insufficiency, such as frequent nausea and vomiting (5) Our patient presented with anorexia, nausea, vomiting and an unintentional weight loss of 13 kg in the past 3 months. Sclerotherapy was performed for a Mallory-Weiss tear in the esophagus detected by endoscopy. IAD is a rare but important condition that may cause hyponatraemia without hyperkalaemia (4). Since low sodium levels have been reported in 88% of patients with primary adrenal insufficiency and in 28% of IAD patients, cortisol levels should be measured in patients with hyponatraemia of unknown etiology (6).

**Conclusion**

In IAD, which is a rare disorder of unclear etiology and difficult to diagnose, all the symptoms may improve with early diagnosis and treatment.

**References**