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Primary Adrenal Insufficiency Misdiagnosed as Hypothyroidism in a Patient with Polyglandular Syndrome

[Sikarin Upala](#),^{1,2} [Wai Chung Yong](#),¹ and [Anawin Sanguankeo](#)¹

¹*Department of Internal Medicine, Bassett Medical Center, Columbia University College of Physicians and Surgeons, New York, USA*

²*Department of Preventive and Social Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Address for correspondence: Dr. Wai Chung Yong, Department of Internal Medicine, Bassett Medical Center, 1 Atwell Road, Cooperstown, New York - 13326, New York, USA. E-mail: waichung.yong@bassett.org

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Abstract

Context:

Autoimmune polyglandular syndrome is a rare condition that causes a variety of clinical symptoms due to autoimmune processes involving multiple endocrine organs. Its vague presentation can cause missed or delayed treatment for adrenal insufficiency, resulting in a life-threatening adrenal crisis.

Case Report:

A 21-yr-old man presented with lethargy, hypotension, hyponatremia, hypoglycemia, and an elevated thyroid-stimulating hormone level. He was binge drinking the day before presentation. No significant response to initial treatment with levothyroxine and dextrose occurred. Diagnostic workup later revealed primary adrenal insufficiency. All initial symptoms completely resolved following treatment with hydrocortisone, fludrocortisone, and levothyroxine.

Conclusion:

Autoimmune polyglandular syndrome causes dysfunction of multiple endocrine organs such as the thyroid gland, adrenal gland, and pancreas. Initial diagnosis of APS is crucial and difficult because of its vague, acute presentation, which often involves hypothyroidism and adrenal insufficiency. Delayed treatment of adrenal insufficiency can result in a life-threatening adrenal crisis. A diagnostic workup for adrenal insufficiency should be performed in patients who do not respond to hypothyroidism treatment.

Keywords: Adrenal insufficiency, autoimmune polyglandular syndrome, hypothyroidism

Introduction

Autoimmune polyglandular syndrome (APS) is a rare genetic disease that causes multiple endocrine disorders.[1] Patients with this syndrome may present with dysfunction of multiple endocrine organs.[2] The vague presentation of endocrine dysfunction can cause a delay in both the diagnosis and the treatment of life-threatening conditions. We, herein, present a case of APS in a 21-year-old man whose condition did not respond to initial treatment and in whom a definitive diagnosis was subsequently achieved by workup for hypocortisolism.

Case Presentation

A 21-year-old man with a history of Hashimoto's thyroiditis with hypothyroidism presented to the emergency department for evaluation of an altered mental status. He had been binge drinking the night prior to admission. He was very lethargic, stared blankly, and was unable to respond appropriately to questions. No tremors or heat or cold intolerance was noted. He reported no fever, difficulty swallowing, shortness of breath, muscle or joint pain, headache, vomiting, or excessive thirst or urination. He had no history of drug abuse. He was compliant with taking levothyroxine (200 mcg daily). His family history was unremarkable.

Physical examination revealed a temperature (T) 34.3°C, heart rate (HR) 68/min, respiratory rate (RR) 16/min, and blood pressure (BP) 87/57 mmHg. He was very lethargic, confused, and able to answer only yes-or-no questions. Neurological examination revealed normal cranial nerves. The patient exhibited hyponatremia (128 mEq/L), hypoglycemia (29 mg/dL), and a high thyroid-stimulating hormone (TSH) level (14.31 μ IU/mL). His blood ethanol level was normal (27 mg/dL). Test for other metabolic panel, complete blood count, triiodothyronine and thyroxine levels, head computed tomography, and urine toxicology screening results were all normal.

He was diagnosed with severe hypothyroidism and received 2 L of fluid for resuscitation, 25 g of dextrose, and a single intravenous (IV) dose of 100 mcg levothyroxine at the emergency department. However, he remained lethargic and was less responsive. An endocrinologist was consulted for evaluation. A random serum cortisol level was <1.0 μ g/dL. A 250 μ g adrenocorticotropic hormone (ACTH) stimulation test was <0.1 μ g/dL.

He was diagnosed with primary adrenal insufficiency and received a treatment with IV hydrocortisone. His mental status, generalized fatigue, and metabolic parameters including glucose and sodium levels substantially improved. He was also given oral hydrocortisone and fludrocortisone. APS type 2 (APS2) was suspected based on his history of hypothyroidism and primary adrenal insufficiency. The results of an additional liver function test, anti-GAD65 antibody titer, testosterone level, and plasma renin activity were all within normal limits. The patient had returned to his normal level of activity by the time of the outpatient follow-up and reported feeling much better after treatment with hydrocortisone, fludrocortisone, and levothyroxine.

Discussion

The present case illustrates an example of APS2, the clinical presentation of which may overlap that of primary adrenal insufficiency and hypothyroidism due to autoimmune thyroiditis. The present patient exhibited lethargy, an altered mental status, hypothermia, hypotension, hypoglycemia, an elevated TSH level, and normal thyroxine levels. His symptoms did not improve after receiving thyroid hormone replacement. He was later found to have primary adrenal insufficiency and his clinical symptoms improved after receiving corticosteroid replacement therapy.

Primary adrenal insufficiency is a principal manifestation of APS2.[3] Autoimmune thyroid disease and type 1 diabetes mellitus are also commonly present.[4] The estimated prevalence of APS2 is 1.5-4.5 per 100,000 individuals.[5] Other autoimmune diseases, especially of the skin, stomach, and gonads, may occur with increased frequency in patients with APS2.

The greatest danger associated with APS2 is treatment of the presenting hypothyroid state without recognition of concomitant hypoadrenalism. Hypothyroidism reduces cortisol clearance, and the addition of thyroid hormone replacement increases cortisol clearance.[6] Additionally, hypothyroidism reduces the metabolic rate, thereby, reducing the need for cortisol. The increased metabolic rate accompanying thyroxine replacement increases the requirement for cortisol.[7] Furthermore, a high serum concentration of TSH in the absence of primary thyroid failure can be a feature of adrenal insufficiency. The development of an adrenal crisis due to underlying adrenal insufficiency has been reported after the administration of thyroxine replacement therapy to patients initially thought to have only hypothyroidism. [8,9,10]

The management of APS2 is based on individualized, lifelong replacement therapy for the affected endocrine organs plus monitoring for development of insufficiency in other organs or associated conditions. The use of medical alert sensors and other measures should be taken to ensure that adrenal function is considered during illness, surgery, or emergency situations. Family members should also be made aware of the increased risk of endocrine disease.

Conclusion

In summary, we have reported a case involving a patient with APS2 who presented with lethargy, hypotension, hypoglycemia, and an elevated TSH level. APS2 is caused by autoimmune processes that affect multiple endocrine organs. This may result in organ damage and a variety of clinical symptoms. The vague presentation of this syndrome can cause missed or delayed treatment for adrenal insufficiency resulting in a life-threatening adrenal crisis.

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Conflicts of interest

There are no conflicts of interest.

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