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CASE REPORT

Relative Adrenal insufficiency masquerading hypothyroidism

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ABSTRACT

A 35 year old male presented with complaints of generalized weakness, easy fatigability and low grade fever for the past 6 months. His past, personal and family history was unremarkable. On examination, his temperature was found to be normal, his pulse was 108/min regular and his blood pressure was 98/60 mmHg in the supine posture, with a fall of 20 mm Hg on standing. Oral examination revealed brownish-black pigmentation over the palate, the buccal mucosa and the palmer crease. The respiratory and the cardiovascular system examinations were normal. Investigations revealed haemoglobin of 8 gm% with other normal parameters; normal liver and renal function tests; serum HIV was non-reactive; serum electrolytes were normal; electrocardiogram was suggestive of sinus tachycardia; chest x-ray was normal; Abdominal ultrasonography was unremarkable and Computerized Tomogram of the Adrenal glands was normal. Serum thyroid stimulating hormone was 20.9 mcg/ml, S Free T4 was 1.2 ng/dl, anti-thyroid Peroxidase antibody was negative and serum cortisol (fasting 8 AM) was 12.0 mcg/dl. The Insulin Tolerance test failed to stimulate cortisol production and hence, the patient was diagnosed as having relative adrenal insufficiency. On treatment with physiological doses of corticosteroids, the patient improved remarkably and his thyroid function test returned to normal within a month.

Key Messages: In patients with relative adrenal insufficiency, elevated TSH values should be dealt with caution and shouldn't be treated as hypothyroidism.

Key Words: Adrenal Insufficiency, Hypothyroidism.

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Introduction

Adrenal insufficiency is an endocrine disorder which is characterized by the deficiency of adrenal steroids. Addison's disease results from progressive destruction of the adrenals, which generally involves more than 90% of the glands before adrenal insufficiency appears [1]. The usual presentation of the disease is with general languor and debility, feebleness of the heart's action, irritability of the stomach and with a peculiar change of the colour of the skin. In developing countries, tuberculosis is found to be the most common cause, whereas idiopathic atrophy with an autoimmune aetiology is found to be the most common cause otherwise[1]. In patients with adrenal insufficiency, Free T4 levels are low to normal, but serum thyroid stimulating hormone (S.TSH) levels are frequently elevated. This elevation in the S. TSH levels usually normalizes with steroid replacement [2].

Case Details

A 35 year old male presented with complaints of generalized weakness, easy fatigability and low grade fever since the past 6 months. The patient also had complaints of anorexia, nausea and weight loss over the past 2 months. There was no history of cough or expectoration. His past history was unremarkable for tuberculosis or chronic illness. He did not have any addiction. His family history was unremarkable for tuberculosis or for autoimmune or heritable disorders. There was no history of extramarital sexual exposure. There was no history of any steroid intake, use of desi (indigenous)

medication or any drug abuse. On examination, his temperature was found to be normal, his pulse was 108/min regular and his Blood Pressure was 98/60 mmHg in the supine posture, with a fall of 20 mm Hg on standing. Oral examination revealed brownish-black pigmentation over the palate, the buccal mucosa and the palmer crease. His respiratory and cardiovascular examinations were normal. Investigations revealed haemoglobin of 8 gm% with normal total and differential counts. The blood indices were normal; liver and renal function tests were normal; S. HIV was non-reactive; serum electrolytes were normal; electrocardiogram was suggestive of sinus tachycardia; chest x-ray was normal; abdominal ultrasonography was unremarkable and Computerized Tomogram of the adrenal glands was normal. S. TSH was 20.9 mcg/ml (0.4-4.2 mcg/ml), S. Free T4 was 1.2 ng/dl (0.3-1.6 ng/dl), anti-thyroid peroxidase antibody was negative and S. Cortisol (fasting 8 AM) was 12.0 mcg/dl. All the hormonal assays were performed by the immuno-chemiluminescence assay.

Because of a strong suspicion of adrenal insufficiency, the patient was subjected to the Insulin tolerance test. The Insulin tolerance test (ITT) was done because of two reasons, the first being that it is still considered to be the 'gold standard' for assessing HPA axis [2] and the second reason being the non availability of Synacthen. Written informed consent was taken before performing the ITT. Fasting Plasma glucose was 98 mg/dl. The Insulin tolerance test was done as per standard protocols. The patient was injected with 0.1 Units of Insulin/Kg body weight and blood glucose analysis was done every 10 minutes. After 30 minutes of insulin injection, the patient's blood glucose was recorded to be 36 mg/dl and the patient developed signs and symptoms of hypoglycaemia. Two blood samples were taken 30 and 60 minutes after the development of hypoglycaemia. The results were as follows – Basal S. Cortisol was 13.0 mcg/dl; S. Cortisol 30 minutes after the development of hypoglycaemia was 15 mcg/dl and S. Cortisol 60 minutes after the development of hypoglycaemia was 10mcg/dl. So, neither the value crossed 18.0 mcg/dl, nor did it increase by more than 7 mcg/dl from the baseline level. Thus, the diagnosis of relative adrenal insufficiency was confirmed.

Considering relative adrenal insufficiency, the patient was started with T. Prednisolone 5 mg in the morning at 8 AM and 2.5 at 4 PM. Within two days, his blood pressure increased to 130/90 mmHg and within one month, the patient was back to his routine work. His general condition improved remarkably and he gained weight by two kg. His oral pigmentation had reduced to minimum. At the end of one month, his S. TSH became 3.96 mcg/ml, thus indicating pseudohypothyroidism and not true hypothyroidism.

Discussion

The incidence of adrenal insufficiency in the general population ranges between 40-60 events/million population. In the intensive care unit, there is a 1-20% incidence pattern depending on how aggressively one looks for it. Adrenal Insufficiency can be divided into: Primary, Central, and Relative. Primary A.I. involves a pathological process within the adrenal gland, leading to the destruction of at least 90% of the gland [3].

Most of the manifestations are due to the deficiency of corticosteroids, but mineralocorticoid deficiency leads to symptoms of hypotension [1]. Axillary and pubic hair may be decreased in women due to loss of adrenal androgens. It is important of recognize this disorder because it can be effectively treated with drugs. The treatment consists of the replacement of adrenal steroids in physiological doses and in most cases, hydrocortisone alone will suffice. The patients should also be instructed to maintain an ample intake of sodium (3–4 g/d). During periods of intercurrent illness, especially in the setting of fever, the dose of hydrocortisone should be doubled [1].

It is known that TSH is falsely elevated in adrenal insufficiency, which usually resolves with the treatment of the primary disease. The possible explanations for elevated TSH in a patient with adrenal insufficiency could be – co-existence of primary hypothyroidism with primary adrenal insufficiency [5], impaired sensitivity of the thyroid gland to TSH in the hypocortisolaemic states [5] or by lowering thyroid hormone production, the body might be reducing metabolism in the hypocortisolaemic states [5]. Patients with

adrenal insufficiency who have mild elevation in S. TSH at presentation and who become euthyroid after corticosteroid treatment have been described [6], [7]. Generally, the TSH elevation is less than 10mcg/ml [8]. On the basis of the clinical practice guidelines from the American association of Clinical Endocrinologists [9], an elevated TSH value that is below 10 mcg/ml and that is associated with a normal free T4 level can be monitored without the initiation of thyroid hormone replacement therapy. In patients with both hypothyroidism and adrenal insufficiency, the adrenal crisis can be precipitated if thyroid hormone replacement is instituted before the initiation of corticosteroid therapy [10].

What is unique to this case, is that even in presence of relative adrenal insufficiency, S. TSH value is more than 20 mcg/ml, which returns to normal (3.96 mcg/ml) with the physiological replacement of corticosteroids alone. Furthermore, the anti-TPO antibody was negative and the return of TSH to normal after steroid replacement rules out other causes of elevated TSH. Even after extensive search on "PubMed" and "Google Search", I could not find a single case report in which a patient having relative adrenal insufficiency had a S. TSH level of more than 10 mcg/ml.

Conclusion

The take home message from the case is 1) Stimulation test (Synacthen or ITT) to be done in strongly suspected cases to rule out relative adrenal insufficiency. 2) In patients with adrenal insufficiency and elevated TSH, it may be prudent to wait before the initiation of the levothyroxine replacement therapy, as the initiation of levothyroxine treatment without steroid replacement may result in adrenal crisis.

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