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Case report of Primary Adrenal Insufficiency

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ABSTRACT

Addison's disease, also known as primary adrenal insufficiency (PAI), is a rare endocrine disorder characterized by a decrease in all three adrenal hormones. This case report describes a 32-year-old female who presented with generalized weakness, fatigue, weight loss, and hyperpigmentation. Based on her symptoms and laboratory findings, a diagnosis of Addison's disease was made. She was started on hormone replacement therapy, and her symptoms improved significantly.

KEYWORDS: Addison's Disease, Hormone Replacement Therapy, Hyperpigmentation, Generalized Weakness, Cortisols

INTRODUCTION

Addison's disease is a rare endocrine disorder with an estimated incidence of 0.8 per million and a prevalence of 40-110 per million in Europe and the US. [1] It is characterized by partial or total destruction of the adrenal cortex, leading to decreased production of cortisol, aldosterone, and androgens. [2] Clinical features can range from generalized weakness and fatigue to life-threatening adrenal crises during stressful events. [3]

Case Presentation

A 32-year-old female presented with complaints of generalized weakness and fatigue for three years. She had multiple consultations and received various multivitamins and calcium supplements, but her symptoms weren't resolved. She also had hyperpigmentation of the lips, palmar creases, and knuckles, for which she was administered vitamin B12 injections, but the hyperpigmentation persisted. Later, she presented to the outpatient department (OPD) with similar complaints. After a thorough history, we found that she also had a history of decreased food intake, and weight loss, with multiple episodes of postural hypotension, nausea, and one episode of vomiting at the time of presentation.

There was no history of visual disturbances, headaches, or any other signs of increased intracranial pressure. She had no past history of tuberculosis, diabetes mellitus, thyroid disorders, or any other comorbid illness.

On general physical examination, the patient was conscious, alert, thin-built, appeared weak, and slightly dehydrated. Her pulse was 96 beats per minute (bpm) and low volume, and her blood pressure was 80/60 mmHg in the sitting position. Generalized hyperpigmentation was noted mainly on the lips, palmar creases, knuckles, elbows, and oral mucosa (Figure 1). However, no hyperpigmented or hypopigmented patches were observed. There was no thyromegaly, and the remaining physical examination findings and systemic examinations were normal.

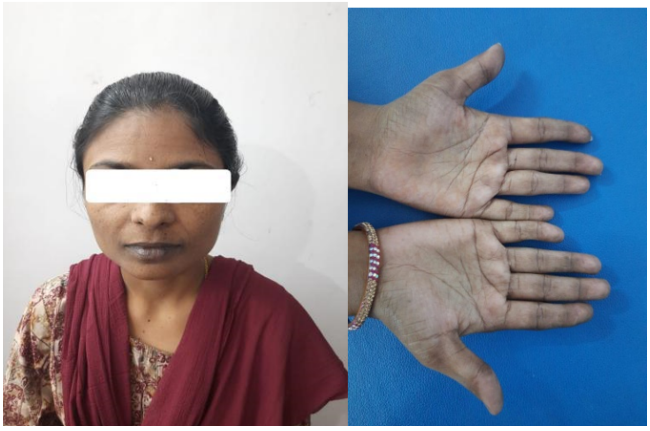

Figure 1: Hyperpigmentation of Lips and Palmar Creases

Routine laboratory investigations showed hemoglobin of 12 g/dL, with normal white blood cell (WBC) and platelet counts. Renal function tests, erythrocyte sedimentation rate

(ESR), serum electrolytes (sodium [Na+], potassium [K+], chloride [Cl-]) at 136/5.4/99, and serum vitamin B12 levels (2000 pg/mL) were all normal. Serum calcium (Ca+2) and phosphorus levels were also normal.

Based on the symptoms of generalized weakness, weight loss, hyperpigmentation, and lab findings of borderline hyponatremia, a differential diagnosis of Addison's disease was suspected. Further investigations were performed accordingly. Early morning 8 am serum cortisol levels were low at 1.02 μg/dL (normal range: 6.02-18.4 μg/dL). Plasma ACTH levels were significantly elevated at 1376 pg/mL (normal: <46 pg/mL). These findings led to a working diagnosis of Addison's disease (primary adrenocortical insufficiency due to decreased cortisol and increased ACTH). A computerized tomography (CT) scan of the abdomen to visualize the adrenals showed normal adrenal glands without any evidence of calcification or focal lesions (Figures 2 and 3).

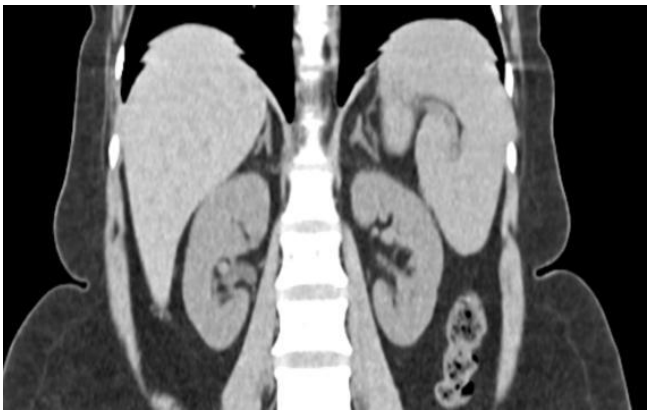

Figure 2: CECT Abdomen Showing Normal Adrenal Glands

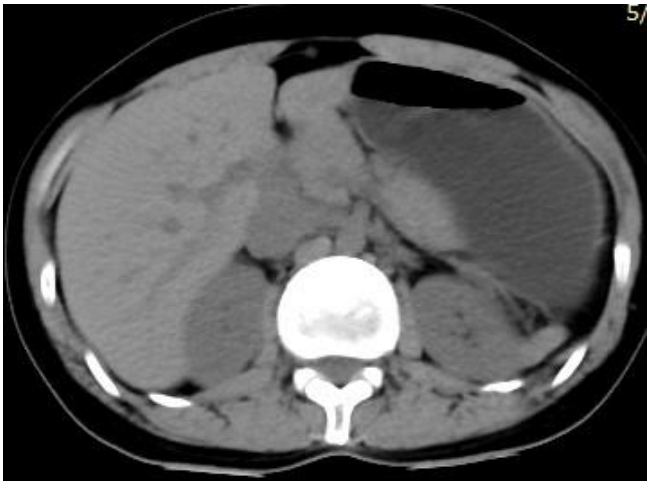

Figure 3: CECT Abdomen Showing Normal Adrenal Glands (Cross sectional view)

Additional laboratory investigations were done to rule out autoimmune polyendocrinopathies. Thyroid function tests revealed T3 of 158.8 ng/dL (normal range: 60-181), T4 of 9.17 μg/dL (normal range: 4.6-10.9), and thyroid-stimulating hormone (TSH) level of 2.96 μIU/mL (normal range: 0.35-5.5). Auto-antibodies against adrenal glands weren't done. However, in this case, with the absence of other common etiologies, autoimmune adrenalitis might have been the most likely cause of primary adrenal insufficiency.

The patient was diagnosed with Addison's disease and then started on oral hydrocortisone 5 mg thrice daily and fludrocortisone replacement therapy 0.1 mg once daily. On follow-up, the patient's symptoms significantly improved, including decreased fatigue, postural hypotension, weight gain, and reduced hyperpigmentation (Figure 3). The patient was educated about the need to double the dose of steroids during times of stress, infection, or illness.

DISCUSSION

Causes of Primary Adrenal Insufficiency

Primary adrenal insufficiency (PAI) was first described by Thomas Addison in 1855. [4] The major causes of PAI differ geographically. In the Western world, autoimmune adrenalitis is the leading cause, while tuberculosis remains the most common cause in India. [4]

Autoimmune Adrenalitis: Around 30% of cases of autoimmune adrenalitis present as isolated adrenal insufficiency. The remaining 70% occur as part of autoimmune polyendocrinopathy syndromes (APS). [1]

- APS 1 is characterized by autoimmune polyendocrinopathy, oesophagal candidiasis, and ectodermal dystrophy.
- APS 2 is characterized by autoimmune thyroid disease, vitiligo, premature ovarian failure in women, hypoparathyroidism, and less commonly type 1 diabetes and anaemia. APS 2 is more common than APS 1. Autoimmune adrenalitis is caused by antibodies against 21-hydroxylase.
- Infectious Causes: Infectious causes of PAI include tuberculosis and HIV/AIDS.
- Other Causes: Other causes include infiltrative disorders, metastases, adrenal haemorrhage in meningococcal infection, and adrenoleukodystrophy (due to accumulation of VLCFA). In children, congenital adrenal hyperplasia due to 21-hydroxylase deficiency is the most common cause.

Clinical Presentation of Adrenal Insufficiency

Addison's disease presents with diverse and nonspecific clinical and biochemical features. [1, 5] Fatigue is the most common presenting symptom. Other symptoms include weight loss, gastrointestinal complaints, myalgias, depression [3], and psychosis. All these features are common for both primary and central adrenal insufficiency except for gastrointestinal disturbances, which are more common in primary PAI, possibly due to electrolyte imbalances.

Features specific to primary adrenal insufficiency include postural hypotension, salt craving, and hyperpigmentation. Hyperpigmentation is caused by cortisol deficiency leading to increased production of proopiomelanocortin, a pro-hormone that is cleaved into the biologically active hormones corticotropin (ACTH) and melanocyte-stimulating hormone (MSH). MSH acts on melanocytes to increase melanin production. In some cases of PAI associated with APS, vitiligo may be present.

Laboratory Findings

Laboratory abnormalities in PAI can include hypoglycemia, hyperkalemia, and hyponatremia. [5] Hyponatremia is due to aldosterone deficiency and partly due to increased levels of ADH caused by the loss of cortisol's inhibitory action on ADH. No electrolyte abnormalities are typically seen in central adrenal insufficiency.

Diagnosis of Adrenal Insufficiency

The gold standard for diagnosing Addison's disease is the cosyntropin stimulation test, which measures serum cortisol levels after administration of a small dose of ACTH. A cortisol level below 550 nmol/L is usually considered indicative of adrenal insufficiency. In the absence of this test, a combination of morning cortisol levels and serum ACTH levels can be used for diagnosis.

Plasma renin activity and aldosterone levels should also be measured to assess mineralocorticoid function and differentiate between primary and central adrenal insufficiency.

Once primary adrenal insufficiency is suspected, a contrast-enhanced CT scan of the abdomen should be performed to visualize the adrenal glands for abnormalities such as metastases, infections, or infiltrates. Adrenal calcification or enlargement on abdominal CT are important signs of adrenal tuberculosis. [6]

If the CT scan shows normal adrenal glands, serum VLCFA levels, especially in males, and auto-antibodies against 21-hydroxylase should be measured. Treatment should not be delayed to determine the aetiology.

Treatment of Adrenal Insufficiency

Treatment of PAI involves hormonal replacement therapy. [7] Hydrocortisone is used at a dose of 15-25 mg daily in three divided doses, with the maximum dose given in the morning. Fludrocortisone, at a starting dose of 0.05 mg (which can be increased up to 0.2 mg daily), replaces aldosterone. Adrenal androgen replacement with 25-50 mg of dehydroepiandrosterone once daily may be an option for patients with a lack of energy or loss of libido.

For patients receiving high doses of hydrocortisone, calcium supplementation may be necessary as steroids can hinder bone mineral density. Dose adjustments are made during follow-up visits based on improvements in symptoms and electrolyte disturbances.

Patients should be counselled on increasing their steroid dose during times of illness or stress and educated about the signs and symptoms of acute adrenal insufficiency.

CONCLUSION

Although Addison's disease is rare, it can occur in the general population. A lack of awareness regarding adrenal disorders can lead to delayed or missed diagnoses, resulting in increased morbidity and mortality. Therefore, physicians should maintain

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