CASE REPORT / OLGU SUNUMU

A Rare Symptom and An Important Disease: Hyperpigmentation and Primary Adrenal Insufficiency

Nadir Bir Semptom ve Önemli Bir Hastalık: Hiperpigmentasyon ve Primer Adrenal Yetmezlik

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ÖZ

Amaç

Adrenal yetmezliğin klinik semptomları spesifik değildir ve bu nedenle yanlış tanı yaygındır. Hiperpigmentasyon, primer adrenal yetmezlik tanısı için spesifik bir bulgudur. Bu olgu primer adrenal yetmezlik tanısında hiperpigmentasyon varlığının önemini vurgulamak amacıyla sunuldu.

Olgu:

Bilinen hastalık öyküsü olmayan 66 yaşında erkek hasta acil servisimize halsizlik, bulantı ve kusma şikayetleri ile başvurdu. İlk değerlendirmesinde kan basıncı 71/55 mmHg olarak belirlendi. Fizik muayenede cilt renginde koyulaşma, el ve dilde hiperpigmentasyon görüldü. Fizik muayenede başka anlamlı bulgu saptanmadı. Hastanın laboratuvar bulgularında Adrenokortikotropik hormon (ACTH)> 1250 pg / mL (referans değeri: <46), kortizol 0.54 µg / dL (referans değeri: 4.82-19.5) olarak belirlendi. Hasta primer adrenal yetmezlik tanısı ile hastaneye yatırıldı.

Sonuç:

Açıklanamayan hipotansiyona eşlik eden hiperpigmentasyon, bulantı, kusma ve halsizlik durumunda primer adrenal yetmezlik tanısı akılda tutulmalıdır.

Anahtar Kelimeler: Adrenal yetmezlik, hipotansiyon, hiperpigmentasyon

ABSTRACT

Aim

Clinical symptoms of adrenal insufficiency are nonspecific and thus misdiagnosis is common. Hyperpigmentation is a specific finding for the diagnosis of primary adrenal insufficiency. This case report is presented to emphasize the importance of the presence of hyperpigmentation in the definition of primary adrenal insufficiency.

Case:

A 66-year-old male with no previous history of disease presented to our emergency department with complaints of weakness, nausea, and vomiting. On his initial evaluation, blood pressure was 71/55 mmHg. Physical examination revealed darkening of skin color and increased pigmentation on hands and tongue. There were no other significant findings on physical examination. The laboratory findings of the patient were: Adrenocorticotropic hormone (ACTH)>1250 pg/mL (reference value: <46), cortisol 0.54 µg/dL (reference value: 4.82-19.5). The patient was hospitalized with the diagnosis of primary adrenal insufficiency.

Conclusion:

In cases where hyperpigmentation, nausea, vomiting, and weakness accompanying unexplained hypotension, the diagnosis of primary adrenal insufficiency should be kept in mind.

Keywords: Adrenal insufficiency, hypotension, hyperpigmentation

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Introduction

Adrenal insufficiency is a life-threatening disease, which may stem from either adrenal gland or hypophyseal-hypothalamic causes. Primary adrenal insufficiency is rarely encountered in the emergency department (ED), with an approximate prevalence of 1/10,000 (1). Secondary adrenal insufficiency is two times more common than primary adrenal insufficiency and the most common cause is the use of exogenous corticosteroids. Clinical symptoms of adrenal insufficiency are nonspecific and thus misdiagnosis is common (2).

We present a patient who had multiple hospital admissions due to nonspecific complaints while the underlying etiology was overlooked. In this case report, we aim to emphasize the important points in the diagnosis of primary adrenal insufficiency for emergency physicians.

Case Report

A 66-year-old male with no previous history of disease presented to our ED with complaints of weakness, nausea, and vomiting. He stated that the weakness started one year ago. He also complained of weight loss. The patient had no surgical history and was not taking any medications. On his initial evaluation, vital findings were; blood pressure: 71/55 mmHg, pulse rate 90 beats/min, temperature: 36˚C, oxygen saturation: 98% on room air. Serum glucose level was 98 mg/dl. Physical examination revealed darkening of skin color and increased pigmentation on hands and tongue (Image 1, 2) (Patient consent is provided for images). There were no other significant findings on physical examination. Intravenous fluid and antiemetic treatment were initiated due to vomiting and hypotension. Despite fluid treatment there was no improvement in hypotension. A diagnosis of adrenal crisis was suspected, and 4 mg IV dexamethasone was added to the treatment. The laboratory findings of the patient were: Adrenocorticotropic hormone (ACTH)>1250 pg/mL (reference value: <46), cortisol 0.54 µg/dL (reference value: 4.82-19.5), blood urea level: 107 mg/dL (reference value 10-50), creatinine 2.12 mg/dL (reference value 0.7-1.3), sodium 118 mEq/L (reference value 136-145), potassium 6.3 meq/L (reference value: 3.5-5). Venous blood gas analysis results were: pH: 7.29, lactate: 1.38 mmol/L, bicarbonate: 17.2 mmol/L, base excess (ECF) -8.5 mmol/L. The abdominal ultrasound did not reveal any mass, hydronephrosis or hemorrhage in the kidneys. The patient was hospitalized with the diagnosis of primary adrenal insufficiency.

Discussion

Primary adrenal insufficiency is a clinical condition characterized by inadequate production of cortisol, aldosterone and adrenal androgens. It is associated with low cortisol and high ACTH levels. Secondary adrenal insufficiency is a disorder caused by inadequate secretion of corticotropin-releasing hormone (CRH) or pituitary ACTH, which results in inadequate adrenal stimulation. It is characterized by low plasma cortisol and ACTH levels (2,3). Since mineralocorticoid hormone production is regulated by salt and water metabolism rather than ACTH, mineralocorticoid activity is usually normal in secondary adrenal insufficiency, whereas in primary adrenal insufficiency, it is abnormal (4). We considered primary adrenal insufficiency in our patient because of the low serum cortisol and high ACTH levels and the electrolyte imbalance suggestive of mineralocorticoid deficiency.

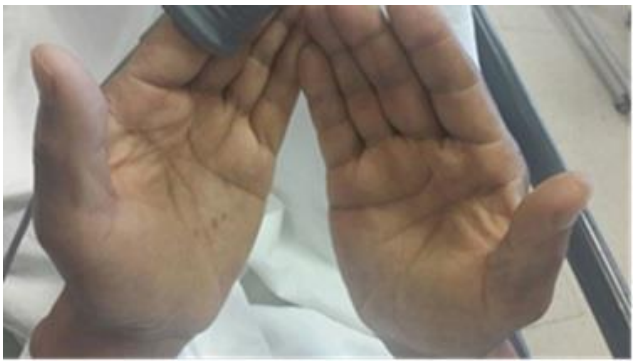

Image 1: Hyperpigmentations in the palm of the left hand.

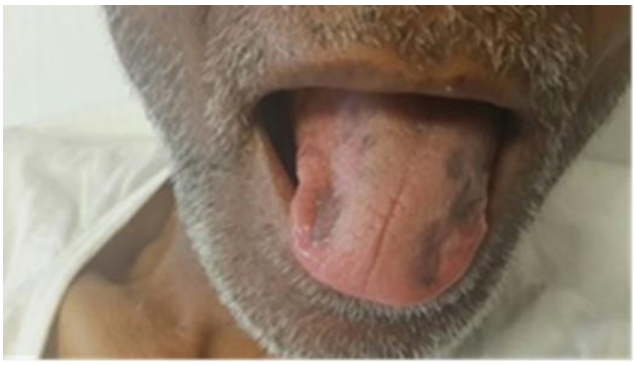

Image 2: Hyperpigmentations on the tongue.

Clinical findings of primary adrenal insufficiency are nonspecific. Weakness, loss of appetite, nausea, vomiting, intestinal cramps, weight loss, low blood pressure, dizziness and salt craving are common complaints (5). However, hyperpigmentation is a more specific finding for the diagnosis of primary adrenal insufficiency, and it is seen in 90% of primary adrenal insufficiencies (3). Increased ACTH concentration leads to melanocyte-stimulating hormone release, which results in black pigment formation in the melanocytes, causing skin and mucosal hyperpigmentation. Hyperpigmentation is most visible on pressure points such as the elbows, joints, palms, lips, and the buccal mucosa (6). In our case, the nonspecific signs and symptoms encountered, such as nausea, vomiting, weight loss, apathy and low blood pressure, were similar to the literature. As a physical examination finding, the primary factor that led us to the diagnosis of primary adrenal insufficiency was the increased pigmentation on the skin and mucosal areas.

Primary adrenal insufficiency diagnosis may be delayed because of the nonspecific physical examination findings and symptoms. Routine laboratory test findings may include hypoglycemia, hyponatremia, normocytic normochromic anemia, eosinophilia, leukopenia, lymphocytosis, hyperkalemia and metabolic acidosis. It is suggested that basal plasma ACTH and serum cortisol levels should be measured before 9 am in patients with suspected adrenal insufficiency. Early morning cortisol levels<4 μg/dL are very supportive for the diagnosis of adrenal insufficiency (3). In addition, rapid ACTH test, insulin tolerance test, and CRH loading test are used to confirm the diagnosis and to discriminate between primary and secondary adrenal insufficiency (3). In our case, the patient had hyponatremia, hyperpotassemia, acute renal failure, metabolic acidosis and eosinophilia. Because the patient applied at 8:27 am, the measured cortisol and ACTH levels were accepted as morning values. The patient was diagnosed with primary adrenal insufficiency regarding the history, hyperpigmentation, electrolyte disturbances and the cortisol and ACTH levels.

In our case, the patient had recurrent hospital admissions with nonspecific complaints but could not be diagnosed. This was probably due to the absence of circulatory collapse in the patient's previous admissions. Factors accelerating the diagnostic process in our case were the hypotension unresponsive to fluid therapy, the lack of clinical evidence to explain the cause of hypotension and the hyperpigmentations.

Patients with adrenal insufficiency who are not diagnosed timely may apply to the ED with adrenal crisis if they meet the risk factors. Stress factors such as infection, trauma, etc., act as triggers for adrenal crisis in patients with adrenal insufficiency (7). The most important pathophysiological finding of adrenal crisis is circulatory insufficiency. In acute adrenal crisis, 500-1000 ml/hour saline infusion and 100 mg hydrocortisone IV injection should be applied initially. Then an infusion of 100-200 mg hydrocortisone in 5% dextrose should be given for 24 hours or an IV injection of 25-50 mg hydrocortisone should be administered every 6 hours (3). When hydrocortisone is not available, as in our case, dexamethasone 4 mg IV may be given as an alternative to hydrocortisone (2). However, it should be considered that the mineralocorticoid effect may be lacking (8).

Conclusion

Emergency physicians should consider the diagnosis of primary adrenal insufficiency in patients with hyperpigmentation, weakness, nausea, vomiting, weight loss and hypotension.

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Informed Consent Statement: Informed consent form was obtained from the patient for the case report.

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