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Visual Diagnosis in Emergency Medicine

BUCCAL MUCOSA HYPERPIGMENTATION AS A DIFFERENTIAL DIAGNOSIS IN A PATIENT WITH UNDIFFERENTIATED SHOCK

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INTRODUCTION

Adrenal crisis (AC) remains an important cause of mortality in patients with adrenal insufficiency (AI). These crises are difficult to diagnose due to the insidious and nonspecific clinical course of the disease. Here, we present the case of a 41-year-old woman with altered mental status with an episode of AC. The case reveals the importance of a complete clinical examination to reach the diagnosis.

CASE REPORT

A 41-year-old woman with an unremarkable clinical history arrived at the emergency department (ED) with altered mental status. The relative who lived with the patient was interviewed. The relative reported a 6-month history of nausea, vomiting, weight loss of 10 kg, and progressive darkening of the skin. One week before the admission, the patient reported symptoms of intermittent abdominal pain localized in the umbilical region and nonbloody diarrhea. During physical examination, she was noted to have a blood pressure of 80/60 mm Hg, heart rate of 108 beats/min, respiratory rate of 20 breaths/min, temperature of 36.9°C, and generalized skin and oral mucosa hyperpigmentation with predominance on the proximal interphalangeal joints and buccal mucosa (Figures 1 and 2); no signs of peritoneal irritation were observed in the abdominal examination. The laboratory examination revealed low serum sodium and potassium at 129 mmol/L and 5.1 mmol/L, respectively, high serum calcium at 11.1 mg/dL, serum creatinine at 1.6 mg/dL, blood urea nitrogen at 32 mg/dL, and lactate at 1.7 mmol/L.

Antibiotic therapy with i.v. 500 mg metronidazole was administered every 8 h, and resuscitation was performed with i.v. fluids (saline), with no change in blood pressure. Two hours after admission, additional blood draws were obtained and, because of clinical signs and symptoms, an infusion of hydrocortisone was started, with a subsequent improvement in blood pressure and consciousness.

Based on the clinical presentation, a thyroid function test and corticotropin (250 μg) stimulation test were performed. The results of the thyroid function test were within the normal range: thyroid-stimulating hormone was 0.33 IU/mL and free thyroxine was 1.51 ng/dL, cortisol was low at baseline and had a muted response at the 30-min and 1-h measurements (0.203 μg/dL and 0.199 μg/dL, respectively). As such, an AC with primary AI was diagnosed. After administration of i.v. hydrocortisone (100 mg every 8 h), the patient showed clinical improvement in her vital signs and mental status.

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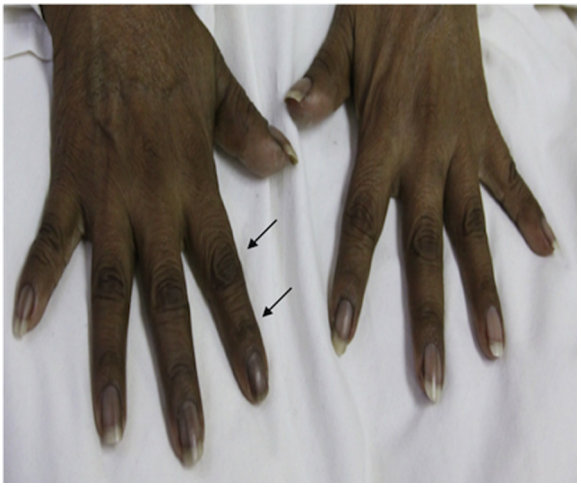

Figure 1. Skin hyperpigmentation with predominance in the area of the proximal and distal interphalangeal joints (indicated by the black arrows).

Oral prednisone and fludrocortisone (at doses of 5 mg twice daily and 0.1 mg per day, respectively) were started, and all i.v. medications were withdrawn. When questioned, the patient confirmed that the darkening of her skin and gums had appeared and progressed in the last 6 months. Before the patient was discharged, a screening test for human immunodeficiency virus (HIV) and tuberculosis infection was performed, and the results were unremarkable.

DISCUSSION

AC is an endocrine emergency that increases patient mortality if not diagnosed and treated promptly. The annual incidence of AC episodes is 5–17% in patients with AI (1). Gastrointestinal infections are the most common cause of AC, while other factors include infections, trauma, and perisurgical and cessation of glucocorticoid therapy. In these patients, hypotension is refractory to the volume of vasoconstrictor agents administered.

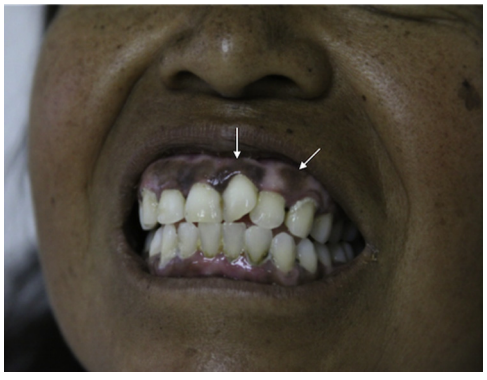

Figure 2. Hyperpigmentation of the buccal mucosa localized in the upper gum area (indicated by the white arrows).

Recognizing the clinical presentation of an AC is of utmost importance because a delay in diagnosis can negatively impact outcomes for the patient (2).

AI is caused by the failure of the adrenal cortex to produce cortisol. This failure can result from a loss of function of the adrenal glands, causing primary AI (PAI), or can be caused by impaired hypothalamic-pituitary regulation of synthesis of adrenal cortisol (secondary AI) (3).

PAI has a prevalence of 93–140 cases per million, although the actual prevalence is unknown because of the misdiagnosis of this disease. Autoimmune adrenalitis (AA) is the most common cause of PAI (68–94% of the cases), while other reported causes are tuberculosis, HIV, fungal infections, and drugs (ketoconazole and rifampin). AA has an isolated presentation in 40% of the cases, while in the remaining cases, it presented in the form of the autoimmune polyendocrine syndrome (4).

AC can be the initial presentation in patients with PAI in 50% of the cases. Patients usually present an insidious evolution of unspecified clinical symptoms, including weakness, anorexia, nausea, vomiting, weight loss, fatigue, reduced consciousness, abdominal pain, diarrhea, orthostatic hypotension, and tachycardia. These symptoms could lead to a misdiagnosis, such as gastroenteritis or acute abdomen; thus, more specific signs and symptoms, such as skin or mucosal hyperpigmentation and salt craving in patients with PAI are relevant. Biochemical abnormalities are also important for the diagnosis of PAI, hyperkalemia, hyponatremia, azotemia, mild hypoglycemia, anemia, hypochloremia, hypercalcemia, and eosinophilia (5).

In PAI, stimulation of melanocytes by the adrenocorticotropic hormones leads to a diffuse pigmentation of the gingiva, tongue, and oral mucosa. The differential diagnosis for a diffuse pigmented lesion of the oral cavity includes, but is not limited to, Peutz-Jeghers syndrome (PJS), Laugier-Hunziker syndrome (LHS), smoker's melanosis, or drug-induced pigmentation. PJS is an autosomal dominant disorder that should be considered in a child or adolescent presenting with diffuse pigmentation of the oral mucosa and gastrointestinal polyposis with a suspicious family history. LHS syndrome is an exclusive diagnosis characterized by darkly pigmented streaks on fingernails and oral pigmentation. Smoking or drug use should also be evaluated. Although microscopic diagnosis is helpful in the diagnosis of focally pigmented lesions, with diffuse presentations we require clinical correlation and time progression of the lesion (6).

In adults, the diagnosis is made by measuring the cortisol level before and 30 min or 60 min after i.v. administration of 250 μg synthetic corticotropin (stimulation test). A peak cortisol level $\leq$ 18 μg/dL (500 nmol/L) at 30 min or 60 min is considered as AI. Guidelines recommend that treatment for a confirmed or suspected

AC should be an immediate parenteral dose of hydrocortisone (100 mg), followed by fluid resuscitation and 200 mg of hydrocortisone in a 24-h infusion or in separate doses (with an interval of 6 h). The infusion must be titrated down, and the enteral treatment should begin with 15–25 mg/day hydrocortisone. If hydrocortisone is unavailable, cortisol acetate, prednisolone, and prednisone can be used as an alternative treatment (7).

If mineralocorticoid replacement is needed, the initiation of fludrocortisone is recommended. It is administered once per day in the morning, usually at the dose of 50–300 μg. Adequate mineralocorticoid replacement is made by measuring the plasma renin concentrations and, if not possible, the dose can be guided with serum electrolytes in normal ranges and with normal blood pressure readings without a substantial postural drop (7).

It is of utmost importance for the emergency physician to recognize the signs and symptoms of an AC as soon as possible because of its high impact on mortality. Patients may arrive at the ED with altered mental status, thus incapable of being interviewed. Taking a few seconds to explore the mouth can make the difference in saving the patient's life.

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