CASE REPORT

A Challenging Case of Addison's Disease

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Abstract

Addison's disease (AD) or primary adrenocortical insufficiency results from hypofunction/dysfunction of an adrenal cortex with a decreased production of mineralocorticoids, glucocorticoids, and androgens, and with increased levels of adrenocorticotropic hormone and plasma renin activity. The AD prevalence is 110–144 cases for every million population among the developed countries.[1]

Autoimmune AD is the most common etiological type in adult patients, which includes about 80% of cases, followed by the second one which is post-tuberculosis AD, seen in 10–15% of the cases, the rest 5% of the cases are caused by neoplastic, vascular, or any rare genetic conditions. The most common form of AD in children is congenital adrenal hyperplasia, and it includes 72% of cases, on the other hand, autoimmune AD is responsible for 10–15% of cases.

Keywords: Addison's disease, Autoimmune, Hyperpigmentation.

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Case History

A 32-year-old mechanic at a shipyard, nonsmoker, nonalcoholic, presented with abdominal pain that had been present for 4 months, along with nausea, vomiting, and weight loss. He presented with skin darkening in a blackish hue over sun-exposed areas, including palms, soles, and buccal mucosa. He had also a history of asexual disturbance in the form of erectile dysfunction for the last 3 months. No history of any drug intake (Fig. 1).

On Examination

Hyperpigmentation was found across sun-exposed areas, including palms, soles, and buccal mucosa, and the patient was aware, oriented, and afebrile. His blood pressure was 100/60 mm Hg in supine position, on standing, 80/60 mm Hg, his pulse rate was 88 beats per minute, his saturation level was 96% at room air, and his systemic examination was normal.

Clinical Diagnosis

- Gastritis
- Hypermelanosis
- Erectile dysfunction

Lab Evaluation

Hb – 12.7 gm/dL
TC – 6500
DC – 48/44/8 ESR – 9/20
Blood sugar – 64 mg/dL
Urea – 35
Creatinine – 1.2
Sodium – 122
Potassium – 5.5
USG abdomen – normal study
Chloride – 93
Calcium – 4.12
Bilirubin – 1.2/0.6/0.6 Sr.

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ADA – 25.81
Mantoux – Negative peripheral smear – Normal ECG – NSR
X-ray chest – Normal
Gastroscopy – Moderate bulbar duodenitis, pan-gastritis, and grade-2 distal esophagitis
CT abdomen – Normal study
USG scrotum – Normal study

Issues

- Generalized black pigmentation.
- Low cortisol and high ACTH.
- Erectile dysfunction – secondary to testicular or pituitary gonadal axis dysfunction.
- Hyponatremia – Euvolemic – Hypoaldosteronism – SIADH.
- Postural hypotension.

How to Proceed Further

Since all his initial investigations were found to be normal, then we planned to evaluate his pituitary hormonal panel, which showed high ACTH and low cortisol levels with low testosterone levels and high TSH with normal FSH, LH, and GH hormones. His ANA was found to be negative (Fig. 2).

ANA – Negative

TFT

T3 – 3.38

T4 – 1.45

TSH – 6.26

Sr. cortisol – 2.30 (4.8–19.5)

ACTH – 700 (6–50 pg/dL)

Sr. testosterone – 1.56 (3.6–11.9)

FSH – 2.14 (1.7–12)

LH – 3.44 (1.1–7.0)

GH – 1.66 (0.03–2.47)

Diagnosis

- Polyglandular disease – involving pituitary, adrenal, and gonads
  AD – primary
- Erectile dysfunction

Differential Diagnosis

- Tuberculosis
- Hemochromatosis
- Sarcoidosis

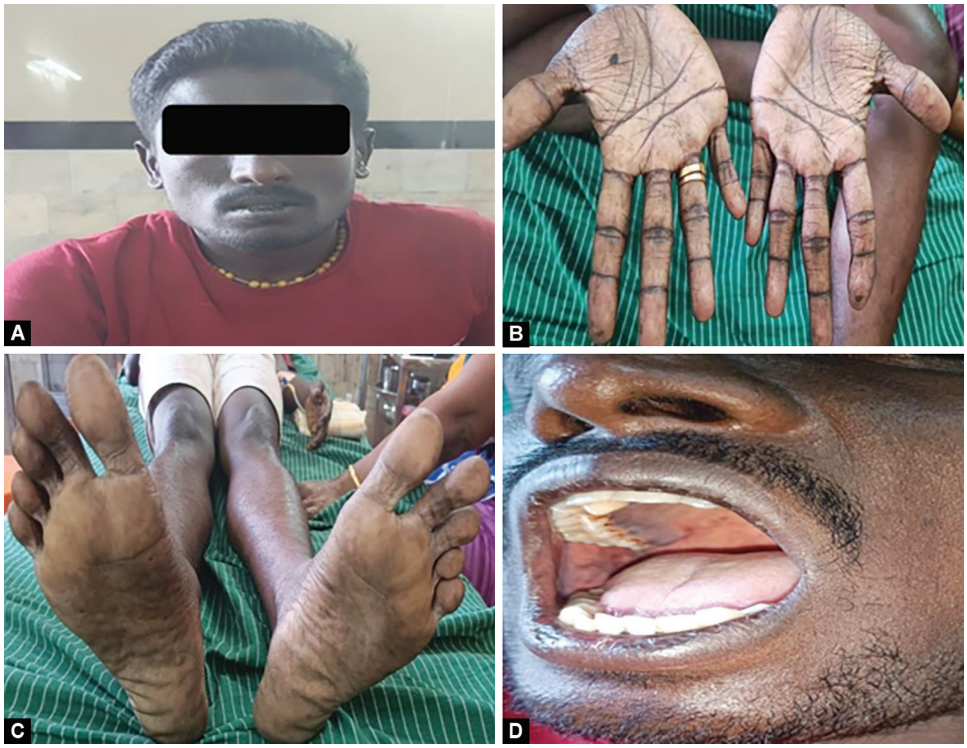
Management

The patient was initially treated with antacids and antiemetics, which relieves his abdominal pain and improved his appetite, but he has persistent postural fall in blood pressure and persistent hyponatremia, hence being treated with hypertonic saline-IV fluid and did not improve. Then, he started on IV steroid hydrocortisone,[2] which improved dramatically, and he continued on oral steroids and supplemented with testosterone injections, which improved his sexual function.[3] He is presently being on follow-up.

Discussion

Addison's disease can be caused by a variety of pathological processes which was first explained by Thomas Addison. Among the most commonest causes of AD are tuberculosis and autoimmune. Many autoimmune pathologies can develop the adrenal insufficiency affecting mainly the adrenal glands or be part of a more complicated inherited polyglandular autoimmune syndrome.[4] The most common cause of AD in developing countries is tuberculosis. Hemochromatosis, fungal infection, metastatic neoplasm, and X-linked adrenoleukodystrophy are also the causes that can lead to AD. Cutaneous and mucosal hyperpigmentations are one of the hallmark signs of AD related to melanogenesis action of ACTH.

Polyglandular-deficiency syndromes (PDS) are characterized by a similar etiology that causes sequential or simultaneous impairments in the function of many endocrine glands. The most common cause is autoimmune disease. Measurement of hormone levels and autoantibodies against damaged endocrine glands is required for diagnosis. Replacement of missing or inadequate hormones, as well as immunosuppressants, is sometimes used in treatment.[5]



Figs 1A to D: (A) Hyperpigmented face; (B) Increased pigmentation in palm creases; (C) Hyperpigmented patches at the sole; (D) Hyperpigmentation at the palate and buccal mucosa

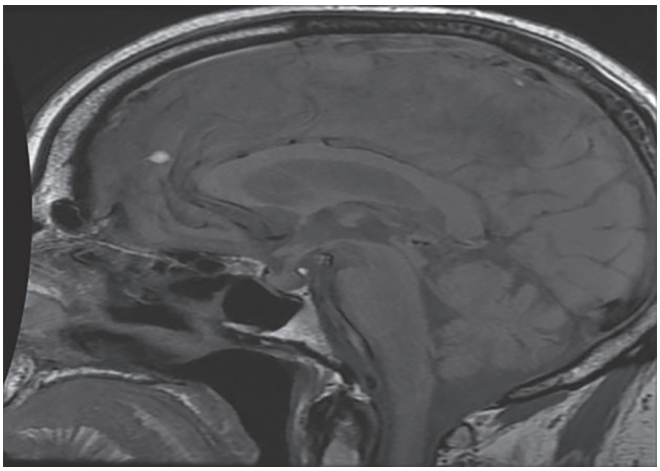


Fig. 2: MRI brain – Enhancing lesion at sellar and suprasellar region—macroadenoma/hypophysitis

Hyperpigmentation in Addison's Disease

- Hyperpigmentation occurs as ACTH and melanocyte-stimulating hormone (MSH) share the same precursor molecule, Pro-opio melanocortin (POMC).
- The POMC of anterior pituitary is cleaved into ACTH, γ-MSH, and β-lipotropin.
- The subunit ACTH undergoes further fragmentation to produce α-MSH, one of the most important MSH required for skin pigmentation.
- In secondary insufficiency of adrenocortical, skin pigmentation does not occur.

Differential Diagnosis of Addisonian Pigmentation

- *Acanthosis nigricans* – intertriginous areas of hyperpigmentation related to insulin resistance.
- Peutz–Jeghers syndrome—a disorder of autosomal-dominant variety manifest as hyperpigmented macules present on the lips and oral mucosa.
- Hemochromatosis (Bronze diabetes)—another common genetic disorder characterized by the chronic gradual accumulation of iron in the body.

Keynotes

- Pigmentation – Addisonian type indicates primary AD.
- Serum cortisol (low) and ACTH (high) levels are diagnostic.
- Persistent hypotension, Hypoglycemia – Suspect Addison's disease.

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