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CONTINUING MEDICAL EDUCATION
ΣΥΝΕΧΙΖΟΜΕΝΗ ΙΑΤΡΙΚΗ ΕΚΠΑΙΔΕΥΣΗ

Endocrinology Quiz – Case 5

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ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2009, 26(3):428–430

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A 35-year-old man was admitted to our hospital for hepatic biopsy due to possible hemochromatosis, based on increased ferritin levels and elevated serum liver enzymes.

Patient's symptoms started eight months ago, when he reported severe gastrointestinal symptoms with abdominal distension and vomiting. Six months ago the patient complained of an unspecified weight loss, weakness, fatigue and hyperpigmentation of the face and the upper and inferior extremities and three months ago about extreme tiredness and vomiting episodes that lasted for 15 days. Initial examination on outpatient basis revealed hypertransaminasemia and he was admitted to the hospital.

There was no history of alcohol abuse or hepatotoxic drug intake. Initial investigations showed the values stated in the table 1. Serological analyses for hepatotropic virus as well as autoantibodies associated with liver were negative, whereas thyroid autoantibodies were strongly positive. Computed tomography scan of the liver revealed increased dimensions of the liver with diffuse fatty liver adiposity infiltration. Both adrenal glands were of small size (1.5 cm). The patient was advised to perform a liver biopsy, therefore was transferred to our hospital.

Physical examination revealed an obese subject (BMI: 31.23 kg/cm^2) with generalized abnormal pigmentation of the skin, especially in sun-exposed areas and knuckles, toes, elbows, and knees, accompanied by increased numbers of black and dark-brown freckles. He had hyperpigmentation of buccal mucosa, gums, tongue and nipples of the breast, areolas, nail beds and palmar creases (fig. 1). He presented with postural hypotension, BP=80/50 mmHg, HR=98/min and without fever. He had sparse axillary hair and very sparse beard growth. The thyroid gland was palpated soft without nodules and increased dimensions. The liver was not palpable. There were no other significant findings. At that time, biochemistry results were as followed in table 1.

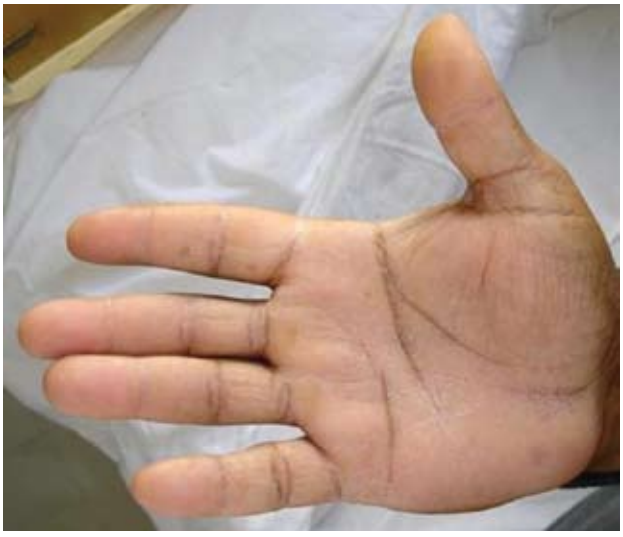

Figure 1

Table 1. Biochemistry results

	Na (mmoL/L)	K (mmoL/L)	ALT (U/L)	AST (U/L)	γ-GT (U/L)	TBil (mg/dL)	ALP (U/L)	LDH (U/L)	CPK (U/L)	Fe (μg/dL)	Ferritin (ng/mL)
Private center			375	309	410						
First admission	118	5.3	269	197	466	1.4	128	522	706	104	640.2
Second admission	126	5.5	213	146	328	0.3	260	682	479	158	484.1

Given the history of constitutional symptoms, hyperpigmentation and hypotension, with abnormal liver biochemistry results, and hyponatremia with hyperkalemia, which is the running diagnosis?

Comment

Differential diagnosis includes alcohol abuse, obesity, diabetes or drug use, viral cause or cirrhosis, autoimmune hepatitis or hereditary metabolic disorders. Endocrine disease can rarely be a cause of these abnormalities, although hypothyroidism and hyperthyroidism are well recognized causes and even more rarely Addison's disease.

The laboratory work up of the patient revealed: ACTH: 1440 pg/mL (nv [natural values]: 9–52); cortisol: 1.6 µg/dL (nv: 5–25). Further investigations showed the following values: FSH: 1.5 mIU/mL (nv: 1–8); LH: 3.9 mIU/mL (nv: 2–12); TotTesto: 1.2 ng/mL (nv: 2.8–8.8); DHEAS: 39 µg/dL (nv: 80–560); SHBG: 17.7 nmoL/L (nv: 20–70); PRL: 27 ng/mL (nv: 3.2–19); GH: 0.4 ng/mL (nv: <5); IGF-1: 95.5 ng/mL (nv: 180–499); subunit A: 0.59 ng/mL (nv: <0.8); TSH: 51 µIU/mL (nv: 0.3–4.2); T4: 69 nmoL/L (nv: 60–160); T3: 3.3 nmoL/L (nv: 0.8–2.7); anti-Tg: 1,094 IU/mL (nv: <115) anti-TPO: 600 IU/mL (nv: <34); PTH: 27 pg/mL (nv: 10–65); insulin: 58.9 µU/mL (nv: 4–16); C-peptide: 5.26 ng/mL (nv: 1.77–4.68).

These findings confirmed hypocortisolism and pointed adrenal glands as the most possible cause. Indeed, MRI of the pituitary gland revealed increased dimensions of the pituitary gland. Further exams were performed to investigate the cause of the primary adrenocortical insufficiency (tab. 2), which revealed: a negative Mantoux test, positive APCA antibodies, positive anti-IA2 [(0.82 U/mL (nv: <0.75)]

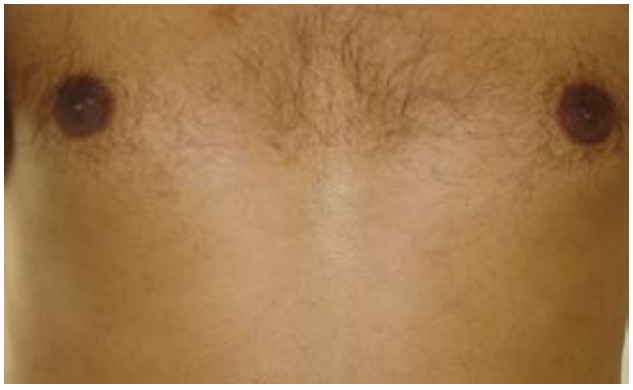

Figure 3

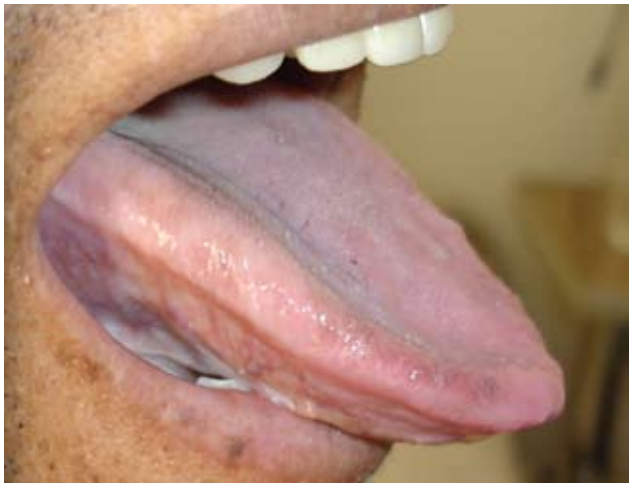

Figure 2

Table 2. Etiologic factors for adrenal insufficiency.

Primary adrenal insufficiency
Autoimmune disease (common)
Isolated
Polyglandular autoimmune syndromes type I and II
Infectious etiologies
Disseminated tuberculosis (common)
Disseminated fungal infections
HIV-infection
Other systemic bacterial infections
Inherited disorders
Adrenal leukodystrophy (rare)
Triple A syndrome
Kearns-Sayre syndrome
Hemorrhagic infarction
Sepsis (meningococcemia/*Pseudomonas aeruginosa)*
Anticoagulant therapy
Antiphospholipid antibody syndrome
Metastatic disease
Iatrogenic
Drugs: ketoconazole, aminoglutethamide, metyrapone, suramin and etomidate
Infiltrative disorders
Congenital adrenal hyperplasia
Congenital adrenal hypoplasia (DAX-1 related forms)
Resistance to ACTH
Secondary and tertiary adrenal insufficiency
Prolonged administration of exogenous corticosteroids (iatrogenic)
Isolated ACTH or CRH deficiency (rare)
Organic hypothalamic or pituitary gland disorders
Primary or metastatic tumors (including macroadenomas and craniopharyngiomas)
Infections
Hypophysitis
Granulomatous-type disorders
Sheehan syndrome
Parasellar lesions (meningiomas)
Prior radiation or neurosurgery
Peripheral resistance to glucocorticoids

and negative anti-GAD 65, ICA antibodies and versus adrenal gland, in order to evaluate for the autoimmune polyglandular syndrome type-2. From these findings the diagnosis of tuberculosis, and autoimmune adrenalitis were excluded.

The clinical picture (gastrointestinal symptoms, hypotension, hyperpigmentation), the laboratory testing (low cortisol levels, with high ACTH levels and hyponatremia with hyperkalemia) and the imaging study (small atrophic adrenal glands, with enlarged pituitary gland) confirmed the diagnosis of primary adrenocortical insufficiency. Accordingly, the patient started daily administration of glucocorticoids and mineralcorticoids. After one week, liver enzymes, serum electrolytes and arterial blood pressure were normalized. Additionally, the patient suffered from severe hypothyroidism. In Hashimoto's thyroiditis, in the rare case of concomitant existence of hypothyroidism and Addison's disease, the therapeutic goal is to restore eucortisolism before thyroxine prescription in order to avoid acute adrenal crisis. At that point, he was prescribed daily administration of thyroxine in low doses.

Addison's disease has also been reported as a cause of increased transaminase levels associated with constitutional symptoms and profoundly increased ferritin levels. These changes are fully reversible but may lead to diagnostic confusion and delay in performing a corticosteroid therapy which is vital for the survival of the patient.

References

1. TEN SV, NEW M, MACLAREN N. Clinical review 130. Addison's disease 2001. *J Clin Endocrinol Metab* 2001, 86:2909–2922
2. ARLT W, ALLOLIO B. Adrenal insufficiency. *Lancet* 2003, 361:1881–1893

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