Case Report

Addisons Disease : A rare case

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ABSTRACT

"Addison's disease" - Primary Adrenal Insufficiency is a rare endocrine disorder. This needs to differentiated from secondary adrenal insufficiency where pathology lies in hypothalamus and pituitary gland. Distinction is done on clinical and laboratory grounds. We report a 40years/Mwho presented with non-specific complaints of generalized weakness, easy fatigability and giddiness.

Key words : Addison's disease, secondary adrenal insufficiency

Introduction :

Addison's disease is a rare endocrine disease[1]. It has an incidence of 0.8 per million and a prevalence of 40-110 per million in US and European countries[2]. No data on incidence and prevalence is available from India. It is caused by destruction or dysfunction of adrenal glands. This results in decreased secretion of hormones-cortisol, aldosterone and androgens. The disease is characterized by weight loss, muscle weakness, fatigue, low blood pressure, and sometimes darkening of the skin in both exposed and non-exposed parts of the body.

Primary adrenal insufficiency can be a life-threatening disorder particularly in stressful situations, since cortisol secretion cannot be increased on demand at all.

CASE REPORT :

40 years old male patient, farmer by occupation, came to medicine OPD with complaints of generalized weakness, easy fatigability since 1 year and postural giddiness since 8 months. Gradual progressive nature of symptoms made him to leave field work. No history of bleeding tendencies, syncope, fever, cough, leg swelling, vomiting, tinnitus. On enquiry, history of hyper pigmentation of skin mainly elbows, knees, lips, and oral mucosa over the last 8 months and reduced appetite, weight loss was significant. There was no past history of diabetes, hypertension, tuberculosis, HIV, jaundice, recurrent blood transfusions.

On general physical examination, the patient was conscious, alert, thin built, appeared weak, and slightly dehydrated. Pulse of 88 bpm which was low volume, blood pressure of 100/60 mmHg in the supine position and 80/50 mmHg in the standing position within 3 minutes and a respiratory rate of 22 breaths/min. No pallor, icterus, lymphadenopathy. Generalized hyperpigmentation mainly on face, palmar creases, knuckles, elbows and oral mucosa was noted. Axillary and pubic hair was normal. Fundus examination was normal. Systemic examination was normal.

Hyperpigmentation seen over face, Mucous Membrane, Palmar Creases and Skin

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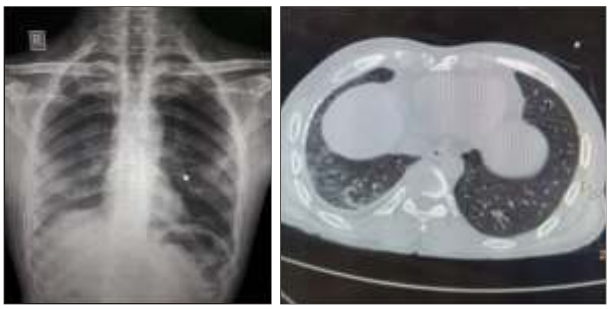
Laboratory investigations showed a hemoglobin of 13.5 g/dl, a total leukocyte count of 8 × 103/μL, Eosinophill counts was 25% (1-4%) and platelet counts were normal. The patient was hyponatremic with a serum sodium of 117 meq/L (135-145 meq/L) and potassium of 4.0meq/L (3.5-5.5 meq/L). Renal and liver function tests were essentially normal. Fasting blood sugar of 102 mg/dL (60-110 mg/dL) and postprandial sugars of 143 mg/dL (80-140 mg/dL) were in the normal range. HbA1c was 5.6 %. Erythrocyte sedimentation rate by Wintrobe method was raised to 37 mm/h (0-9 mm/h). Examination of urine had no significant finding. X-ray Chest showed fibrosis of middle zone on Right lung and ultrasonography of the abdomen showed no significant abnormality. The Mantoux test was negative.

In view of generalized hyperpigmentation, postural hypotension and lab findings of hyponatremia, eosinophilia a differential diagnosis of Addison's disease was kept in mind. Early morning 8 am serum cortisol levels were low 2.641 μg/dl (5-25 μg/dl). Cosyntropin test and serum aldosterone could not be done due to limited resources. Plasma ACTH levels were significantly raised 948 pg/ml (10-46 pg/ml). A working diagnosis of Addison's disease (primary adrenocortical insufficiency owing to decreased cortisol and increased ACTH) was thus made.



CECT adrenal was normal. X-Ray Chest showed pleural thickening and calcification with fibrotic bands on Right lung. Other lab investigation to rule out etiological factors for Addison's disease was done. HIV was non reactive. Sputum for AFB was negative. Free thyroid function tests showed a T3 of 1.43 ng/ml (0.66-1.85), T4 of 8.2 μg/dl (3.2-12.6), a raised thyroid stimulating hormone level of 9.1 mIU/ml (0.5-4.8). Anti TPO, Serum calcium, Serum parathyroid hormone levels were normal. Auto antibodies against adrenal glands and serum levels for light chain fatty acids could not be performed. However, in this case, the absence of other etiologies and suggestive Chest X-ray and CT thorax finding, Tuber cularadrenalitis might have been the most likely cause of primary adrenal insufficiency.

The patient was managed on IV saline infusion and dextrose infusions. The patient was initially put on injectable hydrocortisone 100 mg thrice a day, until he was stabilized. The patient showed improvement. Blood pressure and electrolytes were within normal range by the 3rd day. The patient was discharged on oral prednisolone 5 mg in the morning and 2.5 mg in the evening and fludrocortisone replacement therapy 100 μg once daily as per recommended doses. Patient was also given thyroid replacement with thyroxine 25 μg once a day. On follow-up at 2month, patient showed significant improvement. Blood pressure and electrolytes were within normal range. Thyroid function tests were normal and thyroxine discontinued. Patient again advised to follow up after 2 months with thyroid function test. Patient was counselled about the need to double dose of steroids in times of stress, infection, illness.

DISCUSSION :

In India, tuberculosis is the most common cause for Addison's disease. Autoimmune adrenalitis is more common in the US, out of which 60-70% are due to association with autoimmune polyglandular syndromes (APS). APS Type 1 comprises chronic mucocutaenous candidiasis mainly, hypoparathyroidism rarely lymphomas. APS Type 2 is associated with mainly autoimmune thyroid disease, vitiligo, premature ovarian failure in women, hypoparathyroidism, Type 1 diabetes and pernicious anemia. Other cause of Addison's disease are congenital adrenal hyperplasia, X-linked adrenoleukodystrophy, metastases, lymphomas, hemorrhage secondary to sepsis, fungal infections, HIV, CMV and drugs like mitotane, ketoconazole. Clinical features comprise fatigue (84-95%), loss of appetite (53-67%), weight loss (66-76%), nausea, vomiting and abdominal pain (49-62%), and muscle

and joint pain (36-40%). More specific signs and symptoms are skin hyperpigmentation (41-74%), resulting from enhanced activation of skin melanocortin 1 receptors (MC1R) by high ACTH, and salt craving (38-64%) and postural hypotension (55-68%) due to mineralocorticoid deficiency. Hyponatraemia (70-80%) is the most common laboratory abnormality, followed by hyperkalaemia (30-40%) and normochromic anaemia (11-15%).[3]

Thyroid dysfunction[5] : It is known that TSH is falsely elevated in adrenal insufficiency, which usually resolves with treatment of primary disease. The possible explanations for elevated TSH could be coexistence of primary hypothyroidism, impaired sensitivity of the thyroid gland to TSH in hypocortisolaemic state, or by lowering thyroid hormones, the body might be reducing metabolism. Mild elevation of TSH in addisons disease can be reversed with corticosteroid treatment. Generally, TSH elevation is <10 mcg/ml. American association of clinical endocrinology quotes that TSH < 10 mcg/ml and normal free T4 can be monitored without initiation of thyroid hormones replacement.

To safely establish the **diagnosis** of adrenal insufficiency, an ACTH stimulation test or cosyntropin test should always be performed. Next step is to measure plasma ACTH levels to determine primary or secondary cause of adrenal insufficiency. Plasma renin activity and aldosterone levels should be measured to know the mineral ocorticoid function. Once primary adrenal insufficiency is the likely diagnosis, contrast enhanced CT scan should be done to visualize adrenal glands for metastases, infections, infiltrates. The adrenal calcification and / or enlargement seen on abdominal CT are important signs of adrenal tuberculosis. However, a non-specific or a normal appearance of the adrenals should warrant screening for adrenal auto antibodies and measurement of very long-chain fatty acids in men to rule out adrenol eukodystrophy. Important to note never delay treatment at the cost for diagnosis.[3]

Treatment consists of rehydration, glucocorticoid replacement with IV hydrocortisone 100 mg bolus and 200 mg hydrocortisone over 24 h, till patient improves. Mineralocorticoid replacement therapy can be initiated once the daily hydrocortisone dose has been reduced to < 50 mg. Adrenal androgen replacement is an option in patients with lack of energy, loss of libido. The dose is 25-50 mg dehyrdo-epiandrosterone once daily. All patients need to be counselled for the need for doubling of glucocorticoid oral dose in times of stress, illness and urgent hospitalization. Calcium supplements should be added and bone mineral density should be done. In general, the prognosis for appropriately diagnosed and treated patients with adrenal insufficiency is good.[4]

CONCLUSION :

Many patients visiting with generalised weakness, fatigability since months to years where physician need to consider Addison's disease as one of differential diagnosis. Mortality is due to delayed diagnosis and presentation in crisis.

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