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Case Report

Addison´s disease in a young child: A rare entity in children

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Abstract Addison's disease is an adrenocortical insufficiency due to the dysfunction or destruction of the entire adrenal gland. The disease usually manifests when 90% or more of both adrenal cortices are dysfunctional or destroyed affecting both glucocorticoid and mineralocorticoid functions. The morbidity and mortality associated with Addison´s disease is relatively high due to delay in diagnosis and initiation of therapy. Here, we report a case of a seven years old child who presented to us with diffuse hyperpigmentation of the body, body flexures, palmar creases and mucosae. He was diagnosed with Addison´s disease, which is indeed a rare entity. In addition, this case report will also enhance the importance of cutaneous examination in suspecting Addison´s disease.

Key words
Addison´s disease.

Introduction

Addison's disease is also known as primary adrenal insufficiency. Thomas Addison first described it in 1855 as a syndrome of weakness, fatigue and hyperpigmentation associated with adrenal gland failure.[1] It is a rare disorder that affects 1 in 100,000 of adult population but the incidence of this condition in children is not known.[2] The etio-pathogenesis of Addison's disease has drastically changed from an infectious disease process to autoimmune adrenalitis, however, tuberculosis is still the most predominant cause of Addison's disease in most of the developing nations.[3]

Addison´s disease is difficult to diagnose in early stages and the patient may present with life-threatening adrenal crisis. The symptoms of Addison's disease include chronic worsening fatigue, generalized weakness, postural hypotension, recurring abdominal pain, loss of appetite and gradual weight loss. It may also present with hyperpigmentation of skin, body creases, folds, scars and mucous membranes.[2]

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Case report

A 7 years old boy presented with complaint of increasing pigmentation of skin, anorexia, easy fatigability, weakness and weight loss for last three years. On cutaneous examination, the child looked pale and there was diffuse hyperpigmentation of skin. The pigmentation was more marked in the body flexures, lips, buccal mucosae, gums and post-traumatic scars. The knuckles and palmo-planter creases were also darkened. Systemic examination was unremarkable. There was no history of fever or productive cough and there was no history of tuberculosis in the family. The child looked undernourished with a weight of 16 kg. Clinically, Addison's disease was suspected. There was no family history suggestive of similar disease. Diagnosis was confirmed by morning 8:00 a.m. baseline serum cortisol level which was 0.3 microgram/ dl (normal range is

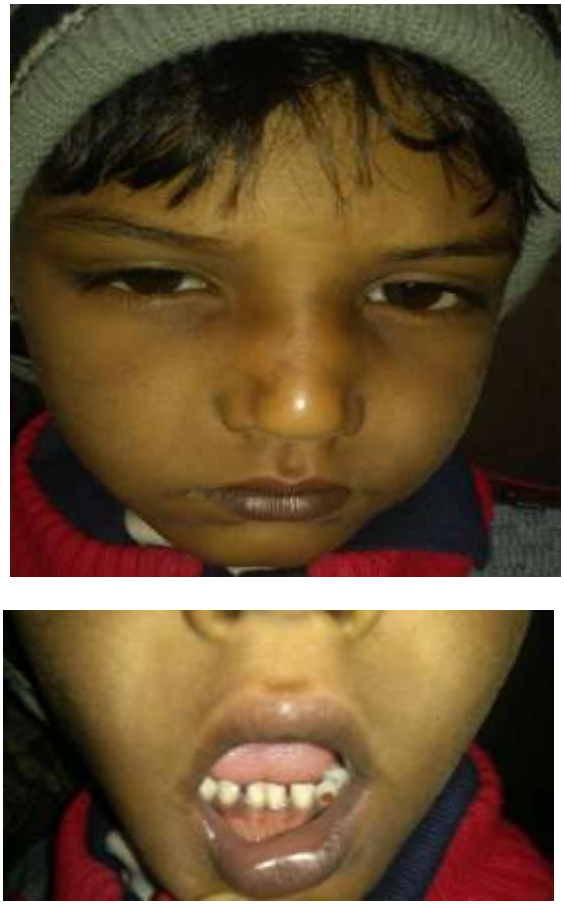

Figure 1 showing pigmentation of face, lips and gums (before treatment)

3.7 to 19.4 microgram/ dl) and serum ACTH level was 609.4 pg/ ml (normal value is up to 46 pg/ml). Other lab investigations showed hemoglobin of 10.2 gm/ dl and MCV 80.6 n. Total and differential leukocyte counts, ESR, lymphocyte count, random blood sugar, blood urea, serum creatinine, serum ferritin, serum calcium and thyroid function tests were all within normal range. Serum electrolytes showed serum sodim 141 mmol/ L, serum potassium 3.9mmol/ L and serum chloride 105 mmol/ L. X-ray chest was normal and Mantoux test was negative. Abdominal ultrasonography of adrenals was normal. CT scan abdomen revealed bilateral adrenal hypoplasia or atrophy along with a small esophageal diverticulum. CT chest was normal. On the basis of clinical characteristics and positive relevant investigations, the diagnosis of Addison´s disease was made and oral prednisolone was started in the dose of 5 mg daily, half in the morning and half in the evening. Parents were advised for regular follow up of child, and to increase the dose of steroids in case of any stressful condition, and to keep a diagnosis card always with the child.

Discussion

The reported incidence of Addison´s disease in adult population is four out of 100,000 people and it is more frequently seen in females than males, and onset is most often seen between the ages of 30 to 40 years.[4] Disease is rarely reported in children but in our case the disease clinically manifested itself in the first decade of life, which is indeed very rare and only few cases are reported in the past in this age group.[4]

Addison's disease is a rare primary adrenocortical deficiency disorder most often caused by autoimmune idiopathic adrenal atrophy or tuberculosis of the adrenal gland. Other causes include surgical removal, hemorrhage, metastatic invasion, parasitic infections, cytomegalovirus, fungal infections and amyloidosis.[5] In our case, the possibility of tuberculosis was ruled out by performing necessary relevant investigations like Mantoux test and CT abdomen. In our case, the low serum cortisol levels, raised serum ACTH levels and bilateral adrenal hypoplasia/ atrophy on CT scan abdomen concludes our diagnosis of primary idiopathic adrenocortical insufficiency. On abdominal CT scan, adrenal calcification and enlargement are important markers of adrenal tuberculosis, therefore, CT scan abdomen should be carried out in all suspected cases of Addisonian-like pigmentation.[5]

It may manifest with a variety of specific and nonspecific clinical characteristics and

biochemical findings.[6] It may present as acute abdomen or neurological manifestations with headaches, depression, and decreased responsiveness.[6] Children may also exhibit a decreased level of activity, weight loss and decline in growth rate.[6]

Our case presented with chief complaints of hyperpigmentation of the skin, body flexures, creases, knuckles, lips and mucosae.[6] Soule *et al*. reported clinical features among fifty patients seen over a 17 year duration study, including darkening of skin and mucosae (86%), loss of weight (67%), abdominal pain (20%) and diarrhea (16%).[7] The increased ACTH levels stimulates melanocytes in the skin, resulting in darkening of skin, flexures, scars and mucosae of the lips, mouth, vagina, rectum and nipples, along with brownish-black freckling over the face, forehead and trunk.[8] Addisonian-like pigmentation can be seen in a wide variety of other disorders like nutritional deficiencies, certain drugs like minocycline, gold salts, antimalarials and other metabolic and endocrine disorders.[8] Therefore, relevant investigations according to the history and clinical characteristics are needed to rule out other pigmentary disorders.

The diagnosis of Addison's disease is ideally possible by the short ACTH stimulation test (consyntropin test) in which the cortisol levels are measured after intravenous or intramuscular administration of ACTH. The cut-off value for insufficiency is usually defined at plasma cortisol levels of less than 550 nmol/ L.[6] Plasma ACTH levels are measured to find out the primary or secondary cause of adrenal insufficiency. Diagnostic findings for patients with Addison's disease includes abnormally low plasma cortisol levels and raised plasma ACTH levels.[6]

Addison´s disease treatment includes replacement of adrenocortical hormones that are hydrocortisone and fludrocortisone.[8] Children are given hydrocortisone 12 to 15 mg/ kg/ day in two doses with $2/3^{rd}$ of the dose in the morning and $1/3^{rd}$ in the evening. Addisonian crisis can occur with any infection or stressful condition therefore, the dose of hydrocortisone needs to be increased.[8] Treatment of this condition needs a combined multidisciplinary effort by involving dermatologists, endocrinologists, paediatricians, neurologists and child psychiatrists particularly, and growth monitoring should be done on regular follow ups.

The wide variety in symptoms means that the diagnosis can be mimicked to other closely related differentials, and the specific features like darkening of skin and mucous membranes can be overlooked, although it may not be always present. So, this case highlights the rare prevalence of this condition in children, and the physicians need to keep a high index of suspicion for Addison's disease especially in children presenting with darkening of skin, flexures and mucosae.

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