

Case Report

Diagnosis and Management of Addison's Disease in a Nulliparous Woman followed by Successful Pregnancy Outcome in a Rural Tertiary Hospital: A Case Report

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Abstract

Introduction: Addison's disease is a relatively rare endocrine condition requiring life-long glucocorticoid and mineralcorticoid replacement therapy. Women with Addison's disease may have a reduced parity. Addisonian crises, a rare but life-threatening event in pregnant women, may accompany stressful conditions such as labor, puerperium, infection, hyperemesis gravidarum or surgery.

Case Presentation: This is a case report of previously healthy 24-year-old nulliparous woman presented with a history of fatigue, fever, diarrhoea and skin darkening. She had pale conjunctiva, low blood pressure, tachycardia, some dehydration, hyperpigmentation of palmer creases, knuckles, buccal mucosa and face. Her serum cortisol was low and rapid ACTH stimulation test with Synacthen showed a poor cortisol response. Patient was immediately managed with IV steroid and later discharged with oral steroid. After 6 months she became pregnant and the steroid therapy was regulated to avoid adrenal crisis during pregnancy. The patient underwent to caesarean section at 38th week and gave birth to a normal baby.

Conclusion: Addisonian crisis represents an endocrine emergency that requires a correct diagnosis with prompt and appropriate salt and steroid replacements to save the patient. Though Addison's disease in women is a risk factor for an adverse pregnancy outcome, it is believed that appropriately treated patients can expect to have uneventful pregnancies of normal duration and without fetal compromise.

Keywords: Addison's disease, Adrenal crisis, Pregnancy, Steroid.

Introduction

Addison's disease, also known as primary adrenocortical insufficiency, is a rare endocrine disease¹ in which there is destruction of the adrenal cortex with resultant inadequate secretion of the adrenal cortical hormones-cortisol, aldosterone and androgens. The symptoms of Addison's disease manifest when more than 90% of the adrenal glands have been destroyed². Patients may present with chronic features and/or in acute circulatory shock. With a chronic presentation, initial symptoms are often misdiagnosed as chronic fatigue syndrome or depression. Adrenocortical insufficiency should also be

considered in patients with hyponatraemia, even in the absence of symptoms³. Pigmentation (dull, slaty, grey brown) is the predominant sign in over 90% of cases⁴. Features of an acute adrenal crisis include circulatory shock with severe hypotension, hyponatraemia, hyperkalaemia and, in some instances, hypoglycaemia and hypercalcaemia. Muscle cramps, nausea, vomiting, diarrhoea and unexplained fever may be present. The crisis is often precipitated by intercurrent disease, surgery or infection³. Treatment should not be delayed to wait for results in patients with suspected acute adrenal crisis.

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A random blood sample should be stored for subsequent measurement of cortisol and, if the patient's clinical condition permits, it may be appropriate to spend 30 minutes performing a short ACTH stimulation test³. Adequate supplement of glucocorticoid and mineralocorticoid are vital for proper management of Addison's disease⁵. Study has proven that women with Addison's disease have a reduced parity compared with other women⁶. Addison's disease has deleterious effects on pregnancy outcome. It may cause infertility, abortion, intrauterine growth retardation, intrauterine fetal death and postpartum adrenal crises^{7,8}. With introduction of glucocorticoid therapy, pregnancy has become less risky for Addisonian women. Maternal mortality has been reduced from 45% of 1930 to 7% of 1948-1955 until to 0.7% of 2000⁹.

Objective

The aim of this report is to describe a case of Addison's disease who became pregnant and successfully gave birth to a healthy baby without a crisis.

Case presentation

In May 2013 a 24-year-old Bangladeshi female presented at KYAMCH, Sirajgonj for evaluation of diarrhoea for 1 day, fever for 15 days, easy fatigability for 1 year. She also noticed increasing darkening of skin and oral cavity for last 4 months. She did not give any history of anorexia, nausea, vomiting, weight loss. Clinical examination revealed pale conjunctiva, low blood pressure as 90/60 mm Hg with postural drop, low volume rapid pulse as 110/ bpm, temperature as 99.5^o F, some dehydration, BMI as 19.29 kg/m², hyperpigmentation of palmer creases, knuckles, buccal mucosa and face. All other systems were essentially normal. Her menstrual cycle was regular. She did not suffer from any chronic illness before and there was no significant drug history. Based upon clinical scenario, investigations were done which revealed hemoglobin 10.7 gm/dl, TC 9.11x10⁹/L, ESR- 30 mm in 1st hour (Western green method), PBF- normochromic normocytic anaemia, RBS- 5.8 mmol/L, hyponatraemia (117 mmol/L), hyperkalaemia (5.6 mmol/L), normocalcaemia (2.25 mmol/L), serum cortisol- 13.9 nmol/L.

Rapid ACTH stimulation test with Synacthen (250 µg i.v.) was done which showed adrenal cortisol insufficiency (serum cortisol at '0' minute-14.60 nmol/L, '30' minute 38.10 nmol/L). Serum ACTH was 684 pg/ml. Meanwhile liver function test, renal function test, chest X-ray, abdominal ultrasound, Mantoux test were

done which showed no abnormalities and no growth were found in blood and urine culture. Adrenal autoantibody, serum aldosterone, plasma renin activity could not be estimated. Based on these scenario, a diagnosis of Addison's disease was done along with acute adrenal crisis. Initially patient was treated with 0.9% normal saline infusion, IV hydrocortisone (400mg/day). Patient's general symptoms improved within 48 hours. Dose of steroid was tapered and she was maintained on oral prednisolone (2.5 mg at 8 am and 2.5 mg at 4 pm). Shortly she was discharged with proper counseling. Steroid card was given with the patient. Subsequent follow up revealed significant improvement of well-being with lightening of the initial hyperpigmentation with no further event of hypotension, fever, diarrhoea and dyselectrolytemia.

After 6 months of diagnosis of Addison's disease the patient became pregnant. During pregnancy she was kept on same drug with same dose. She underwent to ultrasonography at 21st week; biometry was normal (biparietal diameter: 55 mm; occipito- frontal diameter: 68 mm; femur: 41 mm; humerus: 34 mm) and no morphological anomalies were found. In third trimester increased dose of prednisolone was given (5 mg at 8 am and 2.5 mg at 4 pm) and continued till delivery. Her blood pressure, serum electrolytes were normal in all antenatal follow up. At 33rd week the estimated foetal weight was 1830 grams and at 36th week of gestation estimated foetal weight was 2700 grams. Doppler velocimetry was altered in umbilical artery (PI: 1,17) while was normal in middle cerebral artery (PI: 1,48). The patient underwent to caesarean section at 38th week. The newborn, a healthy male baby, weighted 2760 grams and his APGAR was 9/10. During caesarean section 100 mg Hydrocortisone IV was administered to the patient and continued 6 hourly for 24 hours. At follow-up both mother and baby had no health problems and maternal hormonal therapy was changed like pregravidic schedule (2.5 mg at 8 am and 2.5 mg at 4 pm).

Discussion

Thomas Addison (1855)¹⁰ first described the clinical features of primary adrenal insufficiency, which may result from a variety of pathological processes. Hence the term Addison's disease. The characteristic form resulting from primary adreno-cortical insufficiency distinguishes Addison's disease from other forms of adrenal insufficiency which may result from pituitary or hypothalamic diseases,

with decrease in adrenocorticotrophic hormone (ACTH) secretion and consequent adrenal cortex atrophy. Now-a-days, tuberculosis accounts for only 7 to 20 percent of cases of Addison's disease; autoimmune disease is responsible for 70 to 90 percent, with the remainder being caused by other infectious diseases, replacement by metastatic cancer or lymphoma, adrenal hemorrhage or infarction, or drugs¹¹⁻¹⁴. Addison's disease may manifest with diverse and non-specific clinical and/or biochemical features^{1,15}. The most specific sign of primary adrenal insufficiency is hyperpigmentation of the skin and mucosal surfaces associated with fatigue and weight loss¹. Soule reported that the presenting features among patients of Addison's disease seen over a 17-year period, as including hyperpigmentation (86%), weight loss (67%), abdominal pain (20%) and diarrhoea (16%)¹⁵. However, the disease may present atypically, requiring a high index of suspicion for diagnosis^{1,16}. Our patient had increased pigmentation, hypotension, unexplained fever, diarrhoea, hyponatraemia, hyperkalaemia which were characteristic for Addisonian crisis. Short Synacthen test and serum ACTH supported the diagnosis. An "Addisonian crisis" or "adrenal crisis" may be precipitated by trauma, adrenal hemorrhage, intercurrent illness like infection due to insufficiency of adrenal cortical hormones to stress¹⁷. Adequate supplement of glucocorticoid and mineralocorticoid are vital for proper management of Addison's disease⁵. The replacement of glucocorticoid and mineralocorticoid should be continued throughout pregnancy, delivery and lactation. The dose depends upon clinical condition and serum electrolyte level. As free cortisol increases in the 3rd trimester in normal individual, increment of steroid dose is usually required in Addison's disease during the last trimester¹⁸. At the time of delivery parenteral glucocorticoid therapy is administered¹⁸ and the dose is tapered to maintenance dose in 3 days¹⁹. In some instances severe hyperemesis gravidarum may develop during 1st trimester that may require temporary parenteral steroid therapy to avoid precipitation of a crisis¹⁸. In this case, the baby was free from any congenital defect and his development was normal at follow up visit. The normal serum electrolyte level was found in the baby confirmed other reports that there is no evidence of antenatal over activity of fetal adrenals if the mother's adrenocortical hormones are deficient²⁰. However a pregnant woman with Addison's disease is a high risk pregnancy and she needs careful monitoring and frequent followup²¹.



Hyperpigmentation of face



Hyperpigmentation of buccal mucosa

Conclusion

Addison's disease is an uncommon disease with estimated prevalence of 39-60 cases per million population²². Early detection of primary adrenal insufficiency can be difficult, although treatment is usually successful once it is initiated. With appropriate treatment and a few added precautions, people with Addison's disease can lead active lives and have a normal life expectancy²³. Prior to the introduction of steroid therapy, Addison's disease was associated with a high maternal mortality rate. However if it is diagnosed and treated adequately before the pregnancy, adverse effects are uncommon and there is successful maternal and foetus-neonatal outcome^{24,25}.

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