Pregnancy in Addison's Disease

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Summary:

Pregnancy with Addison's disease is very rare. Addison's disease is caused by destruction or dysfunction of the adrenal cortices. A 25 years old lady with Addison's disease receiving chronic treatment with prednisolone (5mg) 1+½+0 tab daily was admitted in 0bs & Gynae Department, BSMMU on 25th October,'09 with 2nd gravida , 38 wks of pregnancy. Caesarean section was done on 26th October, '09. A male baby of 2.5 kg was delivered. Her peroperative and postoperative periods were uneventful. Inj. Hydrocortisone was given peroperatively and postoperatively. Patient was discharged on 7th P.O.D. with above dose of Tab prednisolone.

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Introduction:

Autoimmune destruction of the adrenals is the most common cause of Addison's disease which must involve more than 90% of the glands before adrenal insufficiency appears [1]. It is characterized by chronic deficiency of cortisol, aldosterone and adrenal androgens and causes skin pigmentation that can be subtle or strikingly dark. Volume and sodium depletion and potassium excess eventually occur in primary adrenal failure.At one time, the commonest cause was tuberculosis, with autoimmune destruction of adrenal gland accounting for a minority of cases. The situation is now reversed and patients may have other autoimmune conditions such as pernicious anemia [2]. It usually appears by age 15 years. Partial or late expression of the syndrome is common. The symptoms may include weakness, fatiguability, weightloss, myalgia, arthralgia, fever, anorexia, nausea, vomiting, anxiety and mental irritability due to excess ACTH. Pigmentary changes consist of diffuse staining over nonexposed as well as exposed parts or multiple freckles; hyperpigmentation is especially prominent over the knuckles, elbows, knees, posterior neck, in palmar creases and nail beds. Nipples and areolas tends to be darker. The skin in pressure areas such as the belt or brassiere lines and the buttocks also darkens. The diagnosis of Addison's disease in pregnancy is difficult, because so many of the features of Addison's disease may be associated with normal pregnancy. However, persistence of nausea and vomiting after 20 wks gestation and weight loss should be considered abnormal [3]. On laboratory investigations the WBC count usually shows moderate neutropenia, lymphocytosis and a total eosinophil count over 300/ mcL. Among patients with chronic Addison's disease, the serum sodium is usually low (90%) while the potassium is elevated (65%). Low plasma cortisol(<3mcg/dl) at 8a.m. is diagnostic, especially if accompanied by simultaneous elevation of plasma ACTH level(usually >200pg/ml). Serum DHEA levels are under 1000ng/ml in 100% of patient with Addison's disease. Replacement therapy should include a combination of corticosteroid and minerolocorticoids. In mild cases hydrocortisone alone may be adequate. Most addisonian patient are well maintained on 15- 25 mg of hydrocortisone orally daily in two divided doses, two thirds in the morning and one third in the late afternoon or early evening. Some patients respond better to prednisone in a dosage of about 2-3 mg in the morning and 1-2 mg in the evening. A proper dose usually results in a normal differential white count. Fludrocortisone acetate has a potent sodium retaining effect. The dosage is 0.05-0.3mg orally or every other day. In the presence postural hypotension, hyponatremia, or hyperkalemia the dosage is increased. During pregnancy the prepregnancy dose of cortisone must be maintained unchanged throughout pregnancy, as a reduction, even late in the third trimester, will be followed by the return of Addisonian symptoms. Furthermore any additional stress such as vomiting, infection or haemorrhage must be met by a temporary increase in maintainance dose[4]. For women undergoing elective surgery , stress doses of cortisol should be administered. On the day of surgery , 300mgm of cortisol can be administered, and this dose can be reduced by 50 mg daily until oral glucocorticoid replacement is reinitiated[5]. Before glucocorticoid replacement therapy becomes available, pregnancy in

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patients with adrenal insufficiency was associated with a maternal mortality rate of 77%; when extracts of the adrenal cortex became available, maternal mortality reduced to 30 %. Now with the use of full steroid replacement therapy, pregnancy should be no excess cause of maternal mortality. In patients with treated autoimmune Addison disease, conception, fetal development and delivery should not be problematic. The only consistently recorded fetal complication is intrauterine growth retardation[6].

Case Report:

A 25 years old lady, 2nd gravida was admitted in BSMMU on 25th Oct, 2009 with 38+ weeks of pregnancy with known case of Addison's disease for 6 years .During her antenatal period she was jointly managed by obstetrician (fetomaternal) and endocrinologist. She was on Tab Prednisolone 15 mgm daily. According to the advice of endocrinologist, S. electrolyte, S.cortisol level and APTT was done monthly from 28weeks onwards. Her APTT was high 41.7 sec (control-28sec).Other parameters were normal. Her pregnancy period was uneventful till 34 weeks then she developed diarrhea and went into adrenal crisis and was managed Inj.Hydrocortisone 200mgm I/V stat and 100mgm I/V 8 hourly for 24 hrs. Since then she has been carrying with her an adrenal crisis card. During her first pregnancy she was on Tab Prednisolone. She went into labour at term and developed shock at second stage of labour, delivered a stillborn female baby. She developed postpartum haemorrhage that was managed by condom catheter , inj.oxytocin, prostaglandin E1and shock was managed by volume replacement, blood transfusion and Inj.Hydrocortisone. During this pregnancy elective caesarian section was done at term to avoid stress of labour. A male baby of 2.5 kg was delivered. Adrenal crisis was prevented with Inj.Hydrocortisone 200mg I/V preoperatively and then 100gm I/V 8 hourly for 72hours followed by Tab Prednisolone(5mg daily). In 2003 she developed diarrhea and vomiting and was admitted into ICDDRB. Diarrhoea was not controlled by ORS or I/V fluid. After investigations she was diagnosed as a case of Addison's disease. Since then she is on Tab Prednisolone 7.5 mg daily. She also complaints of red to blackish rash on and off in her body. Her elder sister is suffering from SLE which is also an autoimmune disease.

Discussion:

Pregnancy in Addison's disease is rare. These patient usually suffer from subfertility. Cortisone appeared to cure this patient subfertility. On the other hand modern antibiotics eliminate the spread of tuberculous infection to adrenals, previously the source of one-half of the cases.However , simple atrophy will still provide new cases and irrespective of the causes, cortisone will so enhance the wellbeing , fertility and expectation of life.

The well being and life span of patients with Addison's disease have been greatly improved by cortisone & allied substances. Prior to 1951 their average expectation of life was only two and a quarter years or three and a half years depending on whether tuberculous infection or atrophy was the cause but women with Addison's disease can now expect to survive the entire reproductive period and to enjoy almost normal fertility. Pregnancy and in particular labour and its complications were hazardous in the past[7,8]. In one study on 13 cases where cortisone was given[9]. One case reported maternal death among these 13 cases. Two cases reported vomiting at 8 weeks of pregnancy led to admission in crisis and managed by cortisone [10]. Our patient went into crisis at 34 weeks of pregnancy because of diarrhoea and managed with Inj. Hydrocortisone in endocrinology department. One case reported development of post partum haemorrhage three hours after delivery[10]. The patient collapsed and recovery was slow inspite of adequate blood transfusion and large doses of deoxycortisone and aqueous adrenal extract. Cortisone 25 mg was given intramuscularly. In our patient during her first delivery, went into adrenal crisis during 2nd stage of labour. Even after forceps delivery she delivered a stillborn baby and developed postpartum haemorrhage immediately and patient was luckily saved because of prompt management with Inj.Hydrocortisone and Blood transfusion. The pre-pregnancy dose of cortisone must be maintained unchanged throughout the pregnancy, as reduction even late in the third trimester,will be followed by the return of Addisonian symptoms[11]. Furthermore, any additional stress such as need by a temporary increase in the maintainance dose. Studies shows that the adrenals of patients with Addison's disease are unable to secrete additional corticosteroid which are recovered from normal patient during pregnancy[12]. During the last trimester there is a reduction in the demand for additional sodium chloride. When

maintenance therapy has included a mineralocorticoid, this should be curtailed but prompt resumption is required after delivery. This suggest some mineralocorticoid production by the placenta. An adrenal crisis is more likely to develop during the first twenty-four hours after delivery than any other time during the child bearing incident[7]. This results from inability of the adrenals to meet the stress of labour.The loss of biologically active placental steroids has been suggested as an additional factor, but is as yet improved. The muscular exertion of labour may be an important factor. To prevent this reaction cortisone 200mg daily during labour and first 48 hours after delivery is recommended. It should be given as 50mg six hourly, intramuscularly during labour and orally thereafter. The blood pressure as determined by hourly reading is the best guide to the adequacy of the dosage, a fall indicating the need for further cortisone. After the first two days of the puerperium the dose of cortisone is gradually reduced to the previous maintainance level, the blood pressure being checked four hourly [9].

Conclusion:

Patient with Addison's disease can expect a normal life expectancy if their adrenal insufficiency is diagnosed and treated with appropriate replacement doses of corticosteroids and if required with mineralocorticoids. Adrenal crises can occur in patients who stop their medication or who experience stress such as infection, trauma, surgery, pregnancy. Pregnancy with Addison's disease should be managed by obstetrician and endocrinologist. Vomiting and diarrhoea should be managed promptly with injection hydrocortisone. Patient should always carry addisonian crisis card. The delivery must be in tertiary hospital, where stress should be managed by inj. hydrocortisone and postpartum haemorrhage should be managed properly to save the life of the mother.

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