Case Report

Addison's Disease in Pregnancy - A Case Report

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Introduction

Addison's disease (Primary adrenal insufficiency) is a rare and chronic disease of adrenal cortex where there is insufficient production of glucocorticoid and mineralocorticoid.[1] Addison's disease has deleterious effects on pregnancy outcome. It may cause infertility, abortion, intrauterine growth retardation, intrauterine fetal death and postpartum adrenal crises. Diagnosis of Addison's disease during pregnancy may be difficult and require much awareness of the physician. Both Addison's disease and physiological changes in normal pregnancy share some common symptoms such as fatigue, nausea, vomiting, weakness, hyper-pigmentation and hypotension.[2] Early diagnosis and adequate supplement of glucocorticoid and mineralocorticoid are vital for proper management of Addison's disease in pregnancy.[3] Patients should be counseled appropriately regarding medication, life-style and precautions to be taken in case of infection, operation or any other stress. They should be advised to contact the health facility if there is any emergency. In this article, we represent a case of Addison's disease in pregnancy where pregnancy was brought to a successful conclusion without any undue complication.

Case Report

A 33 year old Bangladeshi woman was admitted in Bangladesh Medical College and Hospital, Dhaka, on 16.08.2010 as a case of third gravid with 38 week pregnancy with Addison's disease. She was diagnosed as a case of Addison's disease for last two years and was under consultation of an endrinologist. Two years back she was having nausea, vomiting, fatigue, weakness and loss of weight. Hyper pigmentation was also present. At first she was treated by a gastroenterologist without any improvement. Routine investigations and endoscopy revealed no abnormality. Then the physician noted increased pigmentation of skin at pressure points, such as knuckles and feet. He referred her to an endocrinologist. The patient's blood tests did not show the typical change in the serum electrolytes with low sodium and raised potassium levels. Her serum sodium level was 136 mmol/L (Normal range is 135 to 145 mmol/L) and serum potassium level was 4.33 mmol/L (Normal range 3.5 to 5 mmol/L). But her morning serum cortisol level was typically very low (2.90 # mcg/dL where the normal range is 4.2 - 38.4 mcg/dL). Her tuberculin test was negative, thyroid function tests were normal, serum estrogen/ serum luteinizing hormone and serum follicle stimulating hormone levels were elevated. Ultrasound examination of whole abdomen reveals no abnormality. She was diagnosed as a case of Addison's disease and was getting replacement since then.

During pregnancy she was under joint consultation of an endocrinologist and an obstetrician. She was advised to take increased salt and her serum electrolyte was maintained within normal range by increasing dose of glucocorticoid. Before conception she was taking tablet prednosolone (5 mg) at a dose of 1 tablet at 8 am and ½ tablet at 4 pm. During pregnancy the dose of prednisolone was raised to 1½ tablet at 8 am and 1 tablet at 4pm. This dose was maintained till delivery. She was also advised to take oral saline whenever she felt tired.

Her cesarean section was done on 21st August, 2010 under spinal anesthesia. A female baby weighing 2.8 kg was delivered. Injection hydrocortisone 100 mg intravenously 12 hourly was started before induction of anesthesia and maintained for 4 consecutive days. After that, oral prednisolone was continued as before. Her wound healing was normal and puerperium was uneventful. She was breastfeeding her baby satisfactorily. The patient was discharged from hospital on her 5th postoperative day with advice to review after two weeks with serum electrolyte report. She was also advised to maintain the steroid card. Two week follow up report showed normal serum electrolytes, good wound healing and successful breastfeeding. The progress of baby was normal on follow up visit and her serum electrolyte levels were normal.

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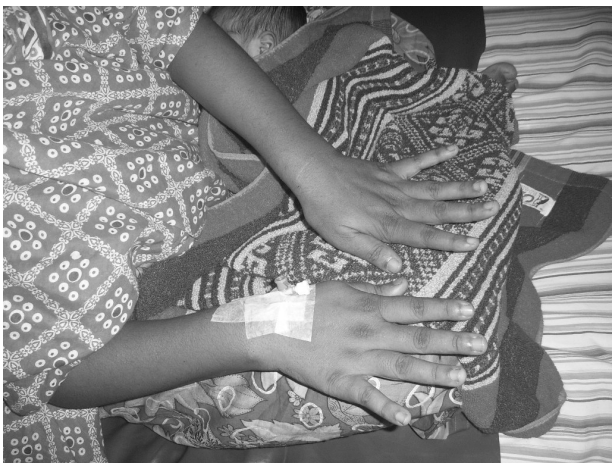

Photograph of The lady with Addison's Disease in Pregnancy Showing Pigmentation of skin at Knuckles

Discussion

As Addison's disease is a rare condition, a direct experience of diagnosis and management of this disease is very rare among general practitioners.[4]

As clinical feature includes non-specific sign symptoms, high degree of suspicion is required for diagnosis. Low serum cortisol and inappropriate diurnal variation, short synacthem test and ACTH level may confirm or refute the diagnosis of Addison's disease.[5] But the reference ranges for pregnant and non-pregnant women are not same, as the concentration of corticosteroid binding globulin (CBG) and cortisol in serum as well as urinary free cortisol level increases two to three fold during pregnancy.[6] But the P-ACTH level remains unchanged during pregnancy, so diagnosis of Addison's disease in pregnancy should be based on P-ACTH.[3] A raised plasma ACTH level confirms the diagnosis of Addison's disease.

The presence of adrenal antibodies indicates autoimmune Addison's disease. 21-hydroxylase antibodies are more sensitive (present in 90% cases) than adrenal cortex antibodies. About 30% of them will have antibodies to 17-hydroxylase and side-chain cleavage enzymes.[7]

Maternal anti-adrenal auto-antibodies may cross the placenta, but usually does not cause any fetal or neonatal adrenal insufficiency.[8] Poor fetal outcome, even death may occur in case of severe maternal hyponatremia or metabolic acidosis.[9] The risk of miscarriage is raised if other autoimmune conditions such as anticardiolipin antibodies are associated with Addison's disease.[9]

The replacement of glucocorticoid and mineralocorticoid should be continued throughout pregnancy, delivery and lactation. The dose depends on clinical condition and serum electrolyte level. The increment of dose is usually required during third trimester. During labor adequate hydration should be maintained through intravenous normal saline and glucocorticoid (that is hydrocortisone sodium succinate), given by intravenous route at a dose of 25 mg 6 hourly. At the time of delivery or if the labor is prolonged, high dose parenteral hydrocortisone should be given (100 mg 6 hourly or as a continuous infusion). After delivery, the dose is tapered to a maintenance dose in 3 days.[10] The blood pressure should be measured hourly as it is the best guide to dictate the dose of hydrocortisone. If the blood pressure is low, the dose of cortisone should be raised. Serum electrolytes and blood sugar determinants are not of much value as controls. After the third day puerperium, when the dose of cortisone is gradually reduced to its previous level, the blood pressure should be measured 4 hourly.[11]

Postpartum haemorrhage may be prevented by administration of ergometrine at the end of second stage of labor. Tolerance to analgesic and anesthesia is normal in patients who had received sufficient replacement of glucocorticoid and mineralocorticoid. Satisfactory lactation depends on adequate supply of adrenal glucocorticoids.[11]

In some instances, patient may develop intractable vomiting, which usually occurs in first trimester of pregnancy and may need a slightly increased dose (1 mg/ day) of dexamethasone parenterally. If the patient is unable to take oral medication, 1-2 mg/ day of deoxycorticosterone acetate in sesame oil may be given as mineralocorticoid replacement by intramuscular route.

In this case, the baby was free from any congenital defect and her 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 deficient.[11]

According to results of a Swedish population based cohort study, patients with diagnosed and undiagnosed autoimmune Addison's disease are at increased risk of preterm delivery, intrauterine growth retardation and other unfavorable pregnancy outcome.[12] A pregnant women with Addison's disease is a high risk pregnancy and she needs careful monitoring and more frequent follow up to identify signs of fetal growth retardation which may lead to short and long term consequences for the infant.

Addison's disease may be associated with ovarian insufficiency and it may partly explain low parity in Addison's disease. Potential risk of development

of premature ovarian failure is a real concern, so the patients should be advised to become pregnant as soon as possible, if she desires to be a mother.[13]

Conclusion

Addison's disease is a rare disorder. Because of adverse effects of glucocorticoid deficiency on pregnancy, pregnancy was rare before introduction of synthetic glucocorticoid and mineralocorticoid supplement. Even if conception takes place the ratio of fetal and maternal complication, fetal growth retardation, perinatal mortality and maternal morbidity and mortality were very high (25-45%) before the era of glucocorticoid and mineralocorticoid supplement with availability of substitution therapy, the prognosis of pregnancy in Addison's disease is now much better.[14] More patients with Addison's disease now approach adulthood and become pregnant. So, more awareness regarding the disease is vital for the early diagnosis and appropriate management.

Adequate steroid replacement along with regular follow up before and during pregnancy may allow normal fetal growth and prevent complications of pregnancy, labor and puerperium.[15,16]

Women with Addison's disease should have pre-pregnancy counseling as they constitute much higher risk group for fetal and maternal complications. They should continue their steroid supplement and keep their medical alert steroid card. And they should also maintain close contact with their health care facility.[13] Close monitoring of these patients allows uneventful pregnancy, labor and puerperium and assures a healthy normal baby.

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The undersigned authors hereby declare that the article is original, neither the article nor a part of it is under consideration for publication anywhere else and has not been previously published anywhere. We have declared all vested interests. We have meticulously followed the instructions. The article, if published, shall be the property of the Journal and we surrender all rights to the Editor. We agree to provide the latest follow-up of case prior to the publication of case report when requested.

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