Familial Hypoparathyroidism with Pregnancy- Challenging Issue for Patient as well as for Physician

MMSU Islam¹, S Mubin², MN Sarker³, DS Ahmed⁴, RC Barman⁵, FM Siddiqui⁶

Abstract

Familial hypoparathyroidism is a rare cause of hypoparathyroidism. It may be x-linked recessive, autosomal dominant or autosomal recessive. In autosomal dominant hypoparathyroidism there is activating mutation of the calcium sensing receptor leading to inhibition of Parathormone (PTH) secretion at inappropriately low serum ionized calcium level. The disease often manifests in the first decade but may appear later. Clinical signs primarily involving neuromuscular disturbances including generalized seizure. Management of pregnancy in hypoparathyroidism is challenging as both under treatment and over treatment is dangerous for fetus. Treatment of hypoparathyroidism in pregnancy includes combination of oral calcium supplementation with calcitriol with an aim to keep serum calcium within normal range. Here we discussed a case of 21 year pregnant lady with familial hypoparathyroidism with successful delivery of a healthy baby.

Key words: Hypoparathyroidism, Hypocalcaemia, Hyperphosphataemia, Epilepsy.

Case Report

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Familial hypoparathyroidism is a rare cause of hypoparathyroidism. It may be x-linked recessive, autosomal dominant or autosomal recessive. In autosomal dominant hypoparathyroidism there is activating mutation of the calcium sensing receptor leading to inhibition of Parathormone (PTH) secretion at inappropriately low serum ionized calcium level. The disease often manifests in the first decade but may appear later. Clinical signs primarily involving neuromuscular disturbances including generalized seizure. Management of pregnancy in hypoparathyroidism is challenging as both under treatment and over treatment is dangerous for fetus. Treatment of hypoparathyroidism in pregnancy includes combination of oral calcium supplementation with calcitriol with an aim to keep serum calcium within normal range. Here we discussed a case of 21 year pregnant lady with familial hypoparathyroidism with successful delivery of a healthy baby.

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Introduction:

Hypoparathyroidism is an endocrine disorder characterized by a deficiency in PTH, resulting in hypocalcaemia and hyperphosphataemia. Primary hypoparathyroidism is an uncommon endocrine disorder that develops as the result of an absolute or relative deficiency in parathyroid hormone (PTH)¹,². Idiopathic and hereditary hypoparathyroidism are often manifest within the first decade but may appear later³. PTH deficiency causes hypocalcaemia, hyperphosphatemia, decreased levels of vitamin D, and clinical signs primarily involving neuromuscular disturbances including generalized seizure²,⁴,⁵. In normal human pregnancy maternal serum concentrations of 1,25(OH)₂D₃ rise early in the first trimester of pregnancy, remain high and show a further increase during the third trimester. On the third day after delivery they fall to non-pregnant levels⁶,⁷,⁸. PTH concentrations increased from the first to the second trimester, declining again in the third trimester to the levels of the first trimester. However, PTH significantly increased in postpartum period. Calcitriol requirement is increased in women with hypoparathyroidism in the third trimester of pregnancy⁹,¹⁰. Low or undetectable PTH level in the face of hypocalcaemia, hyperphosphatemia, and normal renal function establishes the diagnosis of hormone-deficient hypoparathyroidism¹¹. Treatment of hypoparathyroidism in pregnancy includes combination of oral calcium supplementation with calcitriol. The serum calcium concentration should be kept within the lower normal range (between 2.00 and 2.20 mmol/l), which generally requires a calcitriol dose between 0.25 and 3.00 μg/day. Starting from 0.25μg/day calcitriol and a calcium supplementation of 1 g/day, increasing the dosage after the 20th week of gestation with further elevation in the last trimester². Because of the short half-life of calcitriol, symptomatic tetany at night time may become a problem, which can be controlled by dividing the dose¹². Serum calcium levels should not fall below 1.70 mmol/l to avoid preterm labour or midtrimester abortion¹³.

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Case report:

This patient Mrs. Kulsum was diagnosed as a case of familial hypoparathyroidism 8 years back on 2003 at DMCH during evaluation of tonic clonic seizure while she was a 15 years old girl. She had been suffering from recurrent attacks of tonic clonic seizure since 9 month of age. From 1997 she was on antiepileptics but with poor control of seizure. Along with seizure she also complains of tingling & numbness of distal parts of limbs and peri-oral area from 2002. Her paternal grandmother had epilepsy; among her 6 siblings 5 have recurrent seizure. On examination she had positive Trouseau’s sign. She had hypocalcaemia, hyperphosphatemia and lower serum parathormone level with calcification of bilateral basal ganglia, thalamus, subcortical white matter and cerebellum. After diagnosis she was on oral calcitriol (active vitamin D3), calcium and carbamazepine to maintain normal serum calcium level as well as for seizure control.

Though with good compliance to these medications she is having infrequent attacks of seizure throughout these 6 years period. Within this time she got married and become pregnant on 2008. We followed up her more frequently with measurement of serum calcium and adjustment of calcium and Vitamin D, dose as well as Carbamazepine for seizure control. She was on regular antenatal check up. Despite having infrequent attacks of seizure she continued pregnancy well. She was admitted in BSMMU at 39th week of gestation and delivered a healthy female baby by caesarian section on 04.08.2009. Serum calcium of baby was checked at 7th day and was normal. Her post natal period was uneventful.

Discussion:

Hypoparathyroidism is defined as deficient PTH secretion or action. This condition may lead to overt hypocalcaemia and hyperphosphatemia or it may only predispose to hypocalcaemia in times increased calcium demand, such as pregnancy. Cause of hypoparathyroidism includes surgical removal of glands, destruction by iron or copper overload, autoimmune destruction; parathyroid may fail to develop as a part of DiGeorge's syndrome, inherited mutation in the PTH gene (idiopathic or primary), activating mutation of the calcium sensing receptor leading to inhibition of PTH secretion at inappropriately low serum ionized calcium level (autosomal dominant). Hereditary hypoparathyroidism can occur as an isolated entity or it may occur in association with other abnormalities such as defective development of thymus or failure of other endocrine organs such as the adrenal, thyroid or ovary. Idiopathic and hereditary hypoparathyroidism are often manifest within the first decade but may appear later. A diagnosis can be made based on the presence of hypocalcaemia, hyperphosphatemia and inappropriately low PTH levels as well as exclusion of other causes of hypocalcaemia, especially renal disease. Diagnosis of underlying disease depends on history (e.g., neck surgery), physical findings (e.g., candidiasis, alopecia), and additional laboratory tests (e.g., evidence of hypoadrenalism). Inappropriately elevated urine calcium in subjects with hypoparathyroidism suggests the diagnosis of autosomal dominant hypoparathyroidism. An elevated level of serum PTH measured by immunoassay in a subject with hypocalcaemia, hyperphosphatemia and normal renal function suggests hormone resistant hypoparathyroidism.

Hypoparathyroidism during pregnancy usually presents as a pre-existing condition that the clinician is challenged to manage. The natural history of hypoparathyroidism during pregnancy is confusing due to conflicting case reports in the literature. Some hypoparathyroid women have fewer hypocalcemic symptoms and require less supplemental calcium but some require increased calcitriol replacement in order to avoid worsening hypocalcaemia. Maternal hypocalcaemia must be avoided because it is associated with intrauterine fetal hyperparathyroidism and fetal death. Conversely, over treatment also should be avoided because maternal hypercalcaemia is associated with stillbirth (2%) and neonatal death (2%), neonatal tetany (15%). So, serum calcium level should be maintained within normal range throughout the pregnancy. Late in pregnancy, hypercalcaemia may occur in hypoparathyroid women unless the calcitriol dosage is substantially reduced or discontinued. This effect appears to be mediated by the increasing levels of Parathormone receptor protein (PThRP) in the maternal circulation in late pregnancy.

Treated hypoparathyroidism had no deleterious effects on the pregnancies or newborns. This patient was managed with oral calcitriol and calcium, serum calcium was maintained within normal ranges, despite that she suffered infrequent attack of convulsion. Finally a healthy male baby was born by caesarian section without any complication to mother or newborn.

Conclusion:

Familial hypoparathyroidism is rare entity. Hypoparathyroidism in pregnancy is challenging both for physician and for patient. Both inadequate treatment and over treatment is dangerous for fetus. Frequent monitoring of serum calcium level and maintenance of normal level by adequate vitamin D and calcium supplementation ensures maternal stability as well as prevent fetal complication.
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