

A Case of Primary Hyperparathyroidism-induced Myoclonic Seizure during the Third Trimester of Pregnancy

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Abstract

Primary hyperparathyroidism is very rare during pregnancy, but it may impart significant complications to the mother and fetus. In the second trimester, the treatment of choice is a parathyroidectomy during the pregnancy. However, there is a controversy with regards to surgery during the third trimester. A woman was diagnosed with acute pancreatitis due to hyperparathyroidism at 32 weeks of gestation. Her hypercalcemia was normalized after medical treatment. She was recommended for a surgery. However, she didn't undergo surgery before delivery. She had a tonic-clonic seizure during labor. After a cesarean, the patient underwent a parathyroidectomy, which improved her medical condition. The neonate suffered from neonatal tetany. In this presented case, a refusal to perform this operation might be dangerous for the mother and baby even during the third trimester. Thus, the operative treatment for primary hyperparathyroidism should be considered even in women who are in the third trimester of pregnancy.

Keywords: Primary hyperparathyroidism; Seizure; Pregnancy

Abbreviations

NV: Normal Value; PTH: Parathyroid Hormone; CT: Computed Tomography; MRI: Magnetic Resonance Imaging

Introduction

Primary hyperparathyroidism is a rare condition during pregnancy. Although many cases of primary hyperparathyroidism that are diagnosed during pregnancy are asymptomatic or present with only mild symptoms, symptomatic cases are associated with severe maternal and fetal morbidity and mortality. Maternal complications include constipation, anorexia, nephrolithiasis, bone disease, muscle weakness, pancreatitis, mental changes, and finally, hypercalcemic crisis. In addition, intrauterine growth retardation, prematurity, intrauterine fetal death, and neonatal hypocalcemic tetany may occur in neonates [1]. An exact diagnosis and prompt management are important in order to prevent maternal and fetal complications. For patients with mild hyperparathyroidism, oral phosphates or diuresis with normal saline hydration could be tried. However, recently, surgical parathyroidectomy has become the treatment of choice for patients with hyperparathyroidism during pregnancy. Surgical treatment is strongly recommended especially during the second trimester. However, a parathyroidectomy during the third trimester of pregnancy is controversial because it poses risks for complications associated with general anesthesia, postoperative hypocalcemia, or other obstetric problems [2].

Here we report a case of a pregnant woman who was diagnosed with primary hyperparathyroidism at 32 weeks of gestation who did not receive an operation but who developed a seizure.

Case Report

A 32-year-old woman in her first pregnancy was referred to our emergency room at a gestational time of 32+4 weeks where she presented with abdominal pain that had developed 4 days prior to her visit. On the one hand, she experienced continuous nausea, epigastric tenderness and rebound tenderness. On the other hand, she did not experience diarrhea, vomiting, or costovertebral angle tenderness. Previously, she had no pathologic medical history, and the results of all her antenatal examinations were normal. She had a weight gain of 2

kg during her pregnancy and was normotensive (120/80 mmHg) and afebrile (36.6°C). Blood tests revealed an elevated level of 1980 IU/L of amylase (normal values (NV) 54-168 mmol/L) and an elevated level of 2122 IU/L of lipase (NV 7-60 mmol/L). Her serum calcium level was 15.1 mg/dl (NV 8.2-10.8), her ionized calcium level was 1.72 mmol/L (NV 1.13-1.32) and her parathyroid hormone (PTH) level was 295.2 pg/ml (NV 15-65). Other laboratory tests, including those for serum electrolytes, thyroid function, and liver function, were all consistent with pregnancy. Fetal sonography showed no abnormal findings; however, transabdominal sonography showed hyperechoic medullas in both kidneys, which implied medullary nephrocalcinosis. Sonography of the thyroid revealed a 4.6 cm-sized parathyroid adenoma with cystic changes arising from the left upper parathyroid gland. The parathyroid adenoma was detected by a fine needle aspiration biopsy of the parathyroid gland. The patient was diagnosed with acute pancreatitis and hypercalcemia associated with primary hyperparathyroidism. Treatment began with fasting and hydration with a physiologic saline solution. After conservative treatment for 5 days, her serum calcium level decreased to 12.8 mg/dl. Parathyroidectomy was recommended to the patient, but she refused and wanted to return home. After that, she had not visited our hospital before 37+2 weeks of gestation. At that time, she again refused a parathyroidectomy before delivery. Her calcium level was 12.7 mg/dl, and her ionized calcium level was 1.65 mmol/L at 37+2 gestational weeks. Her Bishop score was just one. Labor was induced with 10 mg Dinoprostone followed by an infusion of oxytocin via hydration. Continuous external fetal heart rate monitoring was applied throughout the labor. The fetal heart rate and the degree of uterine contractions were consistent with normal progress of labor induction. Three hours after oxytocin infusion, the cervix was fully dilated, and the

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fetal station was designated as zero. Suddenly, the patient experienced a tonic-clonic seizure. Self-respiration became impossible, so emergency intratracheal intubation and cardiopulmonary resuscitation was performed immediately. At that time the fetal heart rate was 60 beats/min. An emergency cesarean section was performed within 10 minutes after the development of the maternal seizure. A female baby with a weight of 2600 g was delivered with APGAR scores of 5 and 7 each 1 and 5 minutes after delivery, respectively. After the cesarean delivery, the patient regained consciousness, and her vital signs were stable. A brain computed tomography (CT) scan immediately followed the emergency cesarean section. The CT scan revealed no abnormal findings. She then underwent a left parathyroidectomy ten days after cesarean delivery. Her postoperative serum calcium levels decreased to a physiologically normal range on postoperative day 7 (10.3 mg/dl). One month later, her serum calcium decreased to 7.1 mg/dl which is lower than the values in our reference range. The baby presented with a high serum calcium level (12.8 mg/dl) immediately post-partum. After this point, the serum calcium levels of the baby began to decrease rapidly and reached 5.8 mg/dl at 1 month post-partum, although with aggressive calcium replacement treatment. The baby suffered from transient hypocalcemic tetanus. Thus far, the mother and her baby are in an otherwise normal condition. At the 1 year postpartum visit, neither the mother nor the baby had any complications, and both were doing well.

Discussion

Primary hyperparathyroidism is a rare occurrence in pregnant women. Hunter and Turnbull reported the first case of primary hyperparathyroidism in a pregnant woman in 1939. In the general population, its reported incidence is 0.15% [1]. The exact incidence of primary hyperparathyroidism in pregnant women remains uncertain because approximately 80% of pregnant patients are asymptomatic. However, symptomatic primary hyperparathyroidism in pregnant women can be associated with significant complications for both mother and fetus. The development of complications is linked with the maternal serum calcium level. A serum calcium level of < 12 mg/dl indicates mild hypercalcemia. These patients may be asymptomatic, or may experience mild, nonspecific symptoms including constipation, fatigue, and depression. Patients with moderate hypercalcemia (12 to 14 mg/dl), often experience marked symptoms, such as polyuria, polydipsia, dehydration, anorexia, nausea, and muscle weakness, among others. Patients with severe hypercalcemia (calcium > 14 mg/dl) may have progressive or more severe symptoms including lethargy, confusion, stupor, and coma [1]. During pregnancy, a significant amount of maternal calcium is shunted to the fetus (300 gm/day). Maternal gastrointestinal calcium absorption is increased to facilitate placental calcium transport. The total serum calcium of the mother is decreased, and ionized calcium is decreased after 20 weeks of gestation because of the increased fetal demands for calcium. These changes in maternal serum calcium levels are associated with the physiologic elevation of maternal parathyroid hormone levels [3]. For this reason, the diagnosis of primary hyperparathyroidism during pregnancy is difficult. If the suspected symptoms and signs exist during pregnancy, including nephrolithiasis or pancreatitis, hyperemesis beyond the first trimester, history of recurrent, spontaneous abortions/stillbirths or neonatal deaths, neonatal hypocalcemia or tetany, a total serum calcium concentration greater than 10.1 mg/dl (2.52 mmol/L) or 8.8 mg/dl (2.2 mmol/L) during the second or third trimester, an effort should be made by physicians to render a diagnosis [4]. Maternal hypercalcemia accompanied by hyperparathyroidism may induce fetal hypercalcemia and further suppression of fetal parathyroid function.

After birth, the abrupt interruption of placental transport of calcium results in neonatal hypocalcemia with or without tetany. In the present case, the patient was initially diagnosed with pancreatitis, and only after this was the primary hyperparathyroidism diagnosed. Although the patient was recommended for surgery during the second trimester of pregnancy, she refused to undergo the operation. As a result, she had convulsions during labor, and at that time, she presented with mild to moderate hypercalcemia (Ca 12.7 mg/dl). No abnormal calcification was found in the CT scan of the brain. After an emergency cesarean section, her serum calcium level became closer to the normal range with medical treatment. A parathyroid gland lobectomy was performed at postoperative day 10, and the presence of an adenoma was confirmed after a biopsy. Several cases of primary hyperparathyroidism-induced pancreatitis during pregnancy have been reported [3]. The proposed pathophysiology of pancreatitis due to primary hyperparathyroidism is the deposition of calcium in the pancreatic duct and calcium activation of trypsinogen within the pancreatic parenchyma. It is already well-known that hypocalcemia can contribute to myoclonic seizures [5]. However, there have been few previous reports of pregnant women with primary hyperparathyroidism and seizures [6]. Schnatz and Thaxton cited a 25% incidence of preeclampsia in these patients. Hyperparathyroidism should be considered a risk for preeclampsia [2]. However, the present patient had neither high blood pressure nor proteinuria. The primary symptoms of severe hypercalcemia (>14 mg/dl) induced hypercalcemic crisis are oliguria, anuria, somnolence, and coma rather than myoclonic seizure. Despite that the exact pathophysiology of seizure-like neuropsychiatric manifestations is still unknown; Chen et al. reported that vasoconstriction may play a role in the etiology of hypercalcemia-related seizures [7]. Using magnetic resonance imaging (MRI) and cerebral angiography, they established that hypercalcemia induced reversible vasoconstriction in patients with status epilepticus. After the management of seizures and hypercalcemia, MRI and cerebral angiography revealed a complete reversal of the vasoconstriction. Some authors have mentioned the association between the occurrence of seizures and hypomagnesemia in hypercalcemic patients [6]. However, the present patient's serum magnesium level was 2.0 mg/dl (NV 1.9-3.1) on the day of the operation. The treatment of choice for patients with symptomatic hyperparathyroidism diagnosed during pregnancy is a parathyroidectomy. The maternal risks of parathyroidectomy are minimal, but they include the risks associated with general anesthesia, injury to the recurrent laryngeal nerve, and postoperative hypocalcemia. Surgery should especially be recommended for the patients who are diagnosed in the second trimester [3,4]. If pregnant women are asymptomatic, they may be treated medically with oral phosphates or with diuresis with normal saline hydration. When a diagnosis is made during the first trimester, and their symptoms are tolerable with medical treatment, the patients can be followed-up until the second trimester. At that time, parathyroidectomy should be performed. A controversy exists with regards to whether patients with hyperparathyroidism require a parathyroidectomy during the third trimester of pregnancy or not. In recent years, many authors have reported that operative treatment before delivery should be recommended for pregnant women in the third trimester who have symptomatic hyperparathyroidism [2,8,9]. Recently, some pregnancy women with primary hyperparathyroidism underwent the minimally invasive surgery after preoperative localization procedures during pregnancy in selected cases [10,11]. The patient presented here was diagnosed at 32 weeks of gestation. She was recommended for parathyroidectomy before delivery, but she refused the operation. She had a seizure during labor, and her baby experienced neonatal tetanus after birth. This case supports the opinions that parathyroidectomy

during pregnancy is the preferred treatment even in the third trimester in pregnant women with hyperparathyroidism.

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