

Anesthetic management of primary hyperparathyroidism during pregnancy

A case report

Hong Zeng, MD, Zhengqian Li, MD, PhD, Xiaoqing Zhang, MD, PhD, Ning Wang, MD, Yang Tian, MD, Jun Wang, MD*

Abstract

Rationale: Primary hyperparathyroidism (PHPT) during pregnancy is rare. Nevertheless, hypercalcemia secondary to gestational PHPT may be masked by physiological changes in calcium homeostasis during pregnancy. Gestational PHPT constitutes a serious danger to mother and fetus. Surgery is the only curative treatment when conservative treatment could not control the condition. Due to the lack of guidelines concerning PHPT during pregnancy, the optimal anesthetic management of PHPT during pregnancy needs to be individualized. Patient concerns: We report a case of PHPT with successful surgical treatment under combined cervical plexus block and general anesthesia.

Diagnosis: She was diagnosed with hypercalcemia, PHPT, a possible parathyroid adenoma, and a 19-week intrauterine pregnancy.

Interventions: The patient underwent heparin-free hemodialysis before the surgery in the nephrology department in the presence of a cardiologist. She then received a successful parathyroidectomy under combined bilateral superficial cervical plexus block and general anesthesia in her 19th week of pregnancy.

Outcomes: She was released from the hospital with no maternal or fetal complications on postoperative day 9. A healthy baby boy was uneventfully born at 37 weeks of gestation.

Lessons: We suggest that surgical removal of the lesion after lowering the blood calcium concentration in mid-pregnancy is currently the optimal treatment option for pregnant patients with PHPT. Furthermore, multidisciplinary perioperative management is particularly important.

Abbreviations: CT = computed tomography, Hb = hemoglobin, HC = hypercalcemia, PHPT = Primary hyperparathyroidism, PTH = parathyroid hormone.

Keywords: hypercalcemia, pregnancy, primary hyperparathyroidism

1. Introduction

The prevalence of primary hyperparathyroidism (PHPT) during pregnancy is about 0.5% to 1.4%. Although it is a rare disorder in pregnancy, PHPT may pose considerable risks to mother and fetus.^[1] The diagnosis of PHPT is characterized by an elevated serum calcium concentration associated with an inappropriately normal, or more commonly elevated parathyroid hormone (PTH) level.^[2] In addition, the use of scintigraphy for localizing

the adenoma is impossible, and few drugs are currently available for pHTP during pregnancy. Surgery is the only curative treatment and is recommended when calcium levels are above 2.75 mmol/L. Nevertheless, the life-threatening hypercalcemia (HC) usually presents a serious challenge for both anesthesiologist and surgeon and a thorough planning is needed for a better outcome.^[3] Here, we report a case of PHPT with successful surgical treatment at 19 weeks of gestational age.

2. Case presentation

The committee waived the requirement for approval to conduct this single case study with access to medical records. Informed consent to publication has been obtained from the patient.

A 34-year-old woman (height, 165 cm; weight, 65 kg) was admitted due to a 12-week history of vomiting and a high blood calcium concentration. Her history included a right ovarian cyst diagnosed 1 year previously and a current 17-week intrauterine pregnancy. Her pregnancy check-up 1 month previously showed that her red blood cell count was $1.96 \times 10^9/L$ and hemoglobin (Hb) concentration was 91 g/L. Her follow-up examination after admission showed that her red blood cell count was $2.60 \times 10^9/L$ and Hb concentration was 84 g/L. She was diagnosed with anemia at another hospital but did not receive special treatment.

Editor: N/A.

Jun Wang is the corresponder for this article.

The authors report no conflicts of interest.

Department of Anesthesiology, Peking University Third Hospital, Beijing, China.

* Correspondence: Jun Wang, Department of Anesthesiology, Peking University Third Hospital, No. 49, North Garden Street, Haidian District, Beijing 100191, China (e-mail: luckyoldhorse@sina.com).

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Medicine (2017) 96:51(e9390)

Received: 12 November 2017 / Received in final form: 29 November 2017 /

Accepted: 29 November 2017

<http://dx.doi.org/10.1097/MD.0000000000009390>

She was gravida 2, para 0, and had undergone an induced abortion 1 year previously because the fetus had died in utero.

A physical examination after hospital admission revealed that her blood pressure was 117/75 mm Hg, heart rate was 80 beats/min, and respiratory rate was 18 breaths/min. Laboratory test results showed a blood calcium concentration of 3.95 mmol/L, blood phosphorous concentration of 0.7 mmol/L, Hb concentration of 84 g/L, albumin concentration of 34 g/L, and PTH concentration of 375.30 pg/mL. The thyroid-stimulating hormone and free thyroxine concentrations were both within the reference ranges.

Neck ultrasound revealed a solid nodule measuring $3.2 \times 1.4 \times 1.9$ cm in the right thyroid lobe, indicating possible parathyroid adenoma. The nodule had a clear boundary and rich blood flow within; the surrounding tissues also exhibited rich blood flow. An obstetrics examination indicated that the fetus was in a good condition.

On the basis of the above-described findings, the patient was diagnosed with HC, PHPT, a possible parathyroid adenoma, a 19-week intrauterine pregnancy, and moderate anemia.

Comprehensive treatments included active dilation, promotion of diuresis, administration of salmon calcitonin to lower the blood calcium concentration, and a red blood cell transfusion, all of which reduced the blood calcium concentration to 3.3 mmol/L. The patient was suggested to terminate the pregnancy because of the presence of refractory HC; however, she and her family refused. After consultation with the departments of general surgery, anesthesia, obstetrics/gynecology, endocrinology, and nephrology at our institution, agreement was reached that the patient had indications for surgery. However, because the patient was pregnant, further computed tomography (CT) or radiology examination was not recommended. Accordingly, the available information on the lesion location was insufficient, and the surgical range was undetermined. If an ectopic lesion was present, surgery might not correct the patient's HC condition. Drastic fluctuations in the intraoperative blood calcium concentration might induce symptoms of HC, including severe arrhythmia. The effects of surgical stress and anesthetic drugs on the fetus were unknown. Lowering the blood calcium concentration might cause adverse outcomes, including convulsion and abortion. This information was provided to the patient and her family. Parathyroidectomy under combined cervical plexus block and general anesthesia was scheduled on August 22, 2016.

Physicians from multiple departments discussed the patient's HC and established the following management protocol. The dilation, promotion of diuresis, and administration of salmon calcitonin were continued in the internal medicine department. Preoperative bedside calcium-lowering hemodialysis, intraoperative dynamic monitoring of the blood calcium concentration, preparation for both hemodialysis and lowering of the calcium concentration, and postoperative monitoring in the intensive care unit were also carried out to prevent complications. The anesthetist visited the patient before the surgery. Her preoperative calcium concentration was 3.95 mmol/L, phosphorous concentration was 0.7 mmol/L, and PTH concentration was 375.30 pg/mL. No other systematic abnormalities were observed. The preoperative evaluation revealed a Mallampati class I orientation, New York Heart Association class I cardiac disease, and American Society of Anesthesiologists class III physical status.

At 14:30 on the day of surgery, the patient underwent heparin-free hemodialysis in the nephrology department in the presence of a cardiologist. A post-dialysis follow-up examination performed

2 hours later showed that the serum calcium concentration was 2.33 mmol/L and that the potassium concentration was 2.54 mmol/L. A potassium supplement was administered intravenously. At 16:00, a gastric tube and catheter were placed, and the patient was transferred to the operation room. Next, a peripheral vein was opened and the patient was monitored by noninvasive blood pressure measurement, electrocardiography, and pulse oxygen saturation measurement. The tubing of the noninvasive blood pressure monitor (Vigileo Hemodynamics Monitor; Edwards Lifesciences, Irvine, CA) was placed via the left radial artery to monitor the cardiac index and stroke volume variation. A bispectral index (BIS) anesthesia machine was also connected. Ropivacaine (0.5%) and lidocaine (1.0%) were administered at a final volume of 20 mL to block the bilateral superficial cervical plexus. Under BIS monitoring, sufentanil (15 g), propofol (100 mg), and atracurium (35 mg) were administered intravenously, followed by rapid tracheal intubation with induction. Intermitent positive-pressure ventilation was carried out using the anesthesia machine. Continuous inhalation of sevoflurane (1.5–2.0%) long with application of remifentanil (0.05 g/kg/min) and atracurium (15 mg/h) was facilitated with a pump to maintain anesthesia. Before the skin incision, an arterial blood test showed a calcium concentration of 3.07 mmol/L, PTH concentration of 418.8 pg/mL, blood gas pH of 7.42, PaCO₂ of 39 mm Hg, PaO₂ of 97 mm Hg, potassium concentration of 4.1 mmol/L, ionized calcium concentration of 1.8 mmol/L, glucose concentration of 3.8 mmol/L, bicarbonate concentration of 24.6 mmol/L, hematocrit of 31%, base excess of 0.1, Hb concentration of 102 g/L, and oxygen saturation of 97%. During the surgery, the patient underwent monitoring of her echocardiographic parameters, invasive blood pressure, heart rate, SpO₂, BIS, cardiac output, stroke volume variation, and urine volume; dynamic analysis of her blood gas parameters, PTH concentration, and calcium concentration were also continued. The intraoperative cardiac index and stroke volume variation did not dramatically fluctuate. Follow-up testing 30 minutes after removal of the parathyroid gland showed a calcium concentration of 3.2 mmol/L, PTH concentration of 37.34 pg/mL, blood gas pH of 7.40, PaCO₂ of 38 mm Hg, PaO₂ of 340 mm Hg, potassium concentration of 4.1 mmol/L, ionized calcium concentration of 1.82 mmol/L, glucose concentration of 4.2 mmol/L, bicarbonate concentration of 22.9 mmol/L, hematocrit of 28%, base excess of -1.8, Hb concentration of 92 g/L, and oxygen saturation of 100%. After the surgery, 3 mL of 1% ropivacaine was infiltrated along the neck wound opening. At 19:00, the patient was transferred to the intensive care unit with the tracheal tube in place. The patient had remained under anesthesia for 209 minutes, and the surgery lasted 173 minutes. In total, 750 mL of normal saline was used, 220 mL of urine was collected, and 5 mL of blood was lost. The next day, the tracheal tube was successfully removed.

A follow-up examination on postoperative day 9 showed a PTH concentration of 42.07 pg/mL, calcium concentration of 2.31 mmol/L, potassium concentration of 3.98 mmol/L, sodium concentration of 137.5 mmol/L, and chloride concentration of 106.7 mmol/L. At this time, patient was 20 weeks pregnant, and the fetus had a normal heart with a heart rate of 140 beats/min. The patient was released from the hospital. Figure 1 shows the fluctuation in the blood calcium concentration during her hospital stay.

On December 26, 2016, she was admitted to the hospital again due to placenta previa at 37 weeks of gestation. An emergency cesarean section was performed and a baby boy (weight 2.76 kg; length 45.0 cm; head circumference 33.7 cm, Apgar score 9) was

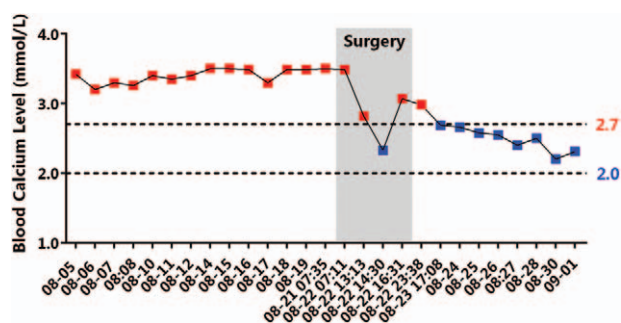


Figure 1. The change of blood calcium concentration during hospitalization.

uneventfully born. The subsequent physical examination of the infant in the neonatal intensive care unit was normal.

3. Discussion

The occurrence rate of PHPT is about 2 to 3 times higher in female than male patients. It is particularly common among middle-aged, postmenopausal women.^[1] Women of childbearing age account for 5% to 10% of all affected patients.^[2] PHPT is the most common cause of pregnancy-related HC. The occurrence rates of relevant complications among pregnant women and their infants are as high as 67% and 80%, respectively.^[3] Complications in mothers include kidney stones, depression, constipation, bone fracture, arrhythmia, pancreatitis, and parathyroid conditions, whereas those in infants include HC, premature birth, slow intrauterine growth, low body weight, neonatal tetany, and even stillbirth.^[3]

3.1. Surgical indications in pregnant patients with PHPT

Nausea, vomiting, constipation, and fatigue secondary to PHPT during pregnancy are easily misdiagnosed as signs of pregnancy. In addition, the limited application of CT or radioimaging during pregnancy makes it difficult to obtain sufficient information about the lesion location, which further increases the risk of a missed diagnosis. Once the diagnosis is clear, the effects of medical treatment might be suboptimal; therefore, whether to select conservative treatment or surgical intervention is the first question faced by clinicians who manage such patients.

Currently, standardized treatment for PHPT during pregnancy is not available. Authors of previous studies have considered parathyroidectomy to be a possible cure for severe HC when conservative treatment could not control the condition.^[4] Surgery is feasible in patients with PHPT in the patients are not pregnant and have normal cardiovascular and kidney function, normal electrocardiograph, and a serum calcium concentration of <3.0 mmol/L.^[5] If a patient has a history of abortion, the surgical criteria might be relaxed; that is, surgery can be considered if the blood calcium concentration is >2.75 mol/L.^[6] The patient in the present study had apparent PHPT symptoms, and her blood calcium concentration remained at 3.3 mmol/L after 2 weeks of medical treatment. She had already undergone 1 abortion. In addition, the patient and her family requested surgical treatment. Therefore, surgery was considered the primary treatment option.

3.2. Surgical timing in pregnant patients with PHPT

Proper surgical timing might lower the risks for pregnant patients and their infants. This is particularly important for pregnant

patients with PHPT. Generally, surgery performed in early pregnancy might affect the development of the organs of the fetus, and surgery performed in late pregnancy might cause premature birth. Therefore, mid-pregnancy (weeks 13–27) is considered the primary surgery window for patients with PHPT.^[4] Norman et al^[7] performed a systematic retrospective analysis of 77 cases of pregnancy combined with PHPT among 32 patients from the previous 6 years. They reported a pregnancy loss rate of 48%, and the loss mainly occurred at 12.2 ± 4.5 weeks, which ranges from the late period of early pregnancy to early mid-pregnancy.^[7] The patient in the present study underwent surgery during week 19 of pregnancy as recommended after consultation with multiple departments of our institution, and the surgery was successful as indicated by the postoperative pathological analysis. The patient's postoperative blood calcium concentration was back to normal and the baby heart was also normal. These results were consistent with what was found by Norman et al^[7] that there was no pregnancy loss among the patients who were 19 weeks pregnant.

3.3. Anesthesia management

The anesthetic options for PHPT-related surgery include cervical plexus block, general anesthesia, or their combination. Given that CT and ^{99m}Tc radioisotope application would introduce radiation-associated risks, lesion localization, and diagnosis in pregnant patients with PHPT depend more on neck ultrasound, which has a sensitivity of 69% and specificity of 94%.^[8] Due to the insufficient information regarding localization and the undetermined surgery range and timing, the patient in the present study underwent general anesthesia with tracheal intubation. Because a cervical plexus block reduces the anesthetic drug dosage, a bilateral superficial cervical plexus block was performed. The remifentanyl dose in the present study was less than half of the routine dose. The intraoperative BIS monitoring enabled precise administration of the induction drug propofol; therefore, its dose was also lower than the routine dose. Sevoflurane, which is the least neurotoxic among the commonly used inhalational anesthetic drugs in the clinical setting, was used to maintain the anesthesia.^[9] The surgery in the present study did not induce significant loss of body fluid; thus, normal saline was used instead of the more commonly used salt-based lactated Ringer solution (which contains calcium chloride at 0.1g per 500mL) to avoid unnecessary effects on the blood calcium concentration.

3.4. Effects of hemodialysis on pregnant patients

Application of heparin-free hemodialysis before the surgery in the present study ensured a low-calcium environment for the whole operative procedure. Whether dialysis is harmful to the fetus remains unknown; however, it lowers the levels of important hormones such as progesterone in pregnant women and might cause uterine contractions and premature birth. The most common complication resulting from dialysis is low blood pressure, which might cause fetal distress.^[10] The preoperative hemodialysis protocol in the present study was jointly decided by physicians from the cardiology and nephrology departments: dialysis at 150 mL/min for 2 hours with a total intubation volume of 4.5 L and dehydration volume of 0.2 L. The mother and fetus were closely monitored during the dialysis process; the mother's blood pressure was stable without postdialysis uterine contractions, and the fetus tolerated the procedures well according to the heart data.

3.5. Blood calcium concentration in pregnant women

Blood calcium mainly exists in 3 forms: 40% is bound to plasma protein (mainly albumin), 50% is present as free cations (Ca^{2+}), and 10% is complexed with other ions such as phosphate, sulfate, and citrate.^[11] Pregnant patients undergo specific physiological changes including increases in the blood volume with consequent blood dilution and hypoproteinemia. The detected level of calcium in complexed form would thus decrease, further affecting the perioperative estimation of the blood calcium concentration. As a result, estimation of the blood calcium concentration in pregnant women must account for the plasma albumin concentration using the following formula: corrected blood calcium concentration = $(40 - \text{albumin concentration}) \times 0.02 + \text{serum calcium concentration}$. The Ca^{2+} cation is the biologically effective form of calcium, and its measurement is not affected. Therefore, measuring the Ca^{2+} cation would help in the perioperative management of blood calcium. The blood calcium concentration determined by the automatic biochemistry analyzer in our clinical laboratory department is the total calcium concentration; conversely, the level determined by the blood gas machine in the anesthesia department is the Ca^{2+} cation concentration. The patient in our study had apparent gastrointestinal tract symptoms, imbalanced calcium and phosphorous concentrations, and preoperative loss of filtered blood electrolytes. Therefore, an OPTI dry blood gas analyzer (Opti Medical Systems, Roswell, GA) was used to analyze the dynamic blood gas levels. The measurement was rapid because the device measured the concentration of calcium cations, which can rapidly and precisely reveal the blood calcium concentration.

4. Conclusion

PHPT during pregnancy is rare and complicated, and personalized management is necessary according to the gestational age, severity of HC, and evaluation of tradeoff between the risks and

benefits. Pregnant patients with severe cases of PHPT, such as the patient described herein, require lowering of the calcium concentration before surgery. In particular, preoperative hemodialysis, which enables the blood calcium concentration to be effectively lowered, is a critical factor for successful surgery. Surgical removal of the lesion in mid-pregnancy is currently the primary treatment option for pregnant patients with PHPT. However, the blood calcium concentration at which surgery should be considered remains under discussion. Therefore, multidisciplinary perioperative management is particularly important.

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