Clin. Lab. 2023;69:XXX-XXX

CASE REPORT

Eclampsia as the First Manifestation of Primary Hyperparathyroidism: a Case Report

Sanqiang Niu [1, 2], Kangjun Yu [1, 2], Weili Wang [1, 2], Beibei Jiao [1, 2], Xianyan Tan [1, 2], Huaili Xin [1, 2], Xiuli Sun [1, 2]

[1] *Department of Obstetrics and Gynecology, Bozhou People's Hospital, Bozhou, Anhui, China*
[2] *Department of Obstetrics and Gynecology, Bozhou Clinical College, Anhui Medical University, Bozhou, Anhui, China*

SUMMARY

Background: **This study aimed to explore the diagnosis and treatment strategies of eclampsia during pregnancy and postpartum acute pancreatitis caused by primary hyperparathyroidism.**
Methods: **This study reported a 26-year-old patient who had maternal eclampsia as her first symptom and was admitted to the hospital. The pregnancy was terminated by cesarean section immediately. Postpartum life-threatening complications, such as severe hypercalcemia and acute pancreatitis, occurred afterward. Following completion of the relevant examination, primary hyperparathyroidism was initially considered to be the cause. Symptomatic treatment is ongoing and will be improved, and the patient will be admitted again for parathyroidectomy.**
Results: **The patient gave birth to a premature neonate via cesarean section. The postpartum diagnosis was primary hyperparathyroidism, for which post-surgical pathology showed a parathyroid adenoma.**
Conclusions: **The clinical manifestations of pregnancy with primary hyperparathyroidism are atypical but may cause serious maternal and fetal complications. Early diagnosis and appropriate treatment can prevent serious prenatal and postnatal complications and foster better pregnancy outcomes.**
(Clin. Lab. 2023;69:xx-xx. DOI: 10.7754/Clin.Lab.2022.220138)

Correspondence:
Kangjun Yu
Department of Obstetrics and Gynecology
Bozhou People's Hospital
No. 616 Duzhong Road
Bozhou 236800
China
Email: ykj150577@126.com

Case Report accepted February 8, 2022

KEYWORDS

eclampsia, hyperparathyroidism, pregnancy, pancreatitis

INTRODUCTION

Primary hyperparathyroidism (PHPT) is the third most common endocrine disorder, which has an incidence rate of about 0.23% to 0.85%, just behind diabetes and thyroid disease [1]. A single parathyroid adenoma is the most common cause of PHPT, accounting for about 80% to 85% of cases, while remaining cases are due to parathyroid hyperplasia, multiple parathyroid adenomas (15%), and parathyroid carcinoma (< 1%) [2]. PHPT during pregnancy is uncommon, and its exact incidence remains unknown due to non-specific findings or lack of clinical manifestations. Reportedly, 23% of pregnant women with PHPT during pregnancy have no clinical symptoms [3], making its diagnosis extremely difficult. About two-thirds of PHPT cases during pregnancy re-

sult in maternal complications, with kidney stones being the most common [4]. Complications also include fractures, pancreatitis, hypercalcemia, and hyperemesis gravidarum [5]. Other complications include hypertension during pregnancy and preeclampsia, which can be observed in 25% of patients [6]. PHPT and preeclampsia are believed to have similarities in endothelial damage, insulin resistance and cardiovascular disorders. Severe PHPT during pregnancy is significantly related to the morbidity and mortality of both pregnant women and fetuses. Early diagnosis and proper management can significantly reduce the occurrence of maternal-fetal complications. Therefore, this case study reports on a patient with primary hyperparathyroidism who had eclampsia as the first symptom as well as postpartum hypercalcemia and acute pancreatitis. Accordingly, this study may provide insight into the clinical diagnosis and treatment of PHPT during pregnancy.

CASE REPORT

A 26-year-old pregnant woman (gravida 2, para 1) suffered from convulsions and loss of consciousness at 33 weeks of gestation, after which she was hospitalized at our department. During transportation, the patient convulsed again with clenched teeth and hands, which the transport medical staff managed with a tongue depressor. Preliminary examination was performed after admission. The patient's blood pressure was found to be as high as 188/120 mmHg. The patient was comatose and had no abnormal vaginal bleeding. Her family members denied her having a history of epilepsy, and she had irregular antenatal examinations during pregnancy. The patient was then given labetalol 20 mg intravenously to lower her blood pressure, magnesium sulfate to relieve the spasm (5 g implosive therapy), and dexamethasone (0.6 mg intramuscular injection) to promote fetal lung maturation. Simultaneously, she was given oxygen by mask and underwent electrocardiographic and fetal heart monitoring. She had unremarkable laboratory examinations and was given a preliminary diagnosis of eclampsia, for which emergency cesarean section was performed. The female neonate was delivered prematurely and had a birth weight of 1,280 g. The birth Apgar score of 1 minute and 5 minutes were 7 and 9, respectively. Our team referred the neonate to the NICU for continued care with the assistance of a pediatrician. Combining the gestational age and birth weight of the newborn, intrauterine growth restriction of the fetus was considered. Due to the patient's critical condition, she was referred to the ICU for observation and management following surgery. The patient's emergency laboratory examination demonstrated abnormal indicators of random urine protein +++, serum Ca^{2+} 4.16 mmol/L, while her brain CT imaging was normal (Figure 1a). Thyroid and parathyroid hormones were checked as she also had high serum Ca^{2+}, which showed that parathyroid hormone (250.70 pg/mL) was significantly increased, while thyroid hormone was within the normal range. Next, a neck ultrasound demonstrated a parathyroid mass of about 17 x 23 mm (Figure 2a). A subsequent parathyroid CT scan showed that the right thyroid lobe had a posterior inferior low-density shadow (22 x 16 mm), which was considered to be a parathyroid adenoma (Figure 2b). She was thus initially diagnosed with parathyroid hyperthyroidism, for which treatment was commenced with a single dose of zoledronic acid (4 mg/d intravenously) and cinacalcet (30 mg/12 hours orally). On the second day following the operation, the patient had obvious pain in the upper abdomen, though the specific tenderness point was unknown. Considering the possibility of secondary pancreatitis, electrolyte and amylase tests were done, which revealed a serum Ca^{2+} of 4.44 mmol/L and blood amylase of 1,719 U/L. At the time, the patient was confused, in a poor mental state, and had obvious upper abdominal tenderness combined with hypercalcemia and markedly elevated amylase, which was highly suspicious of acute pancreatitis due to hypercalcemia. A CT scan of the abdomen was then performed in order to assess the condition of the pancreas, which indicated acute edematous pancreatitis (Figure 1b). Intravenous Q8H infusion of 100,000 units of ulinastatin was then commenced along with a large amount of fluids, anticoagulation, catharsis, and enema treatments. Enteral nutrition was suspended, water fasting and gastrointestinal decompression were changed, and changes in the patient's condition were dynamically observed. The patient's serum Ca^{2+} remained high, and the outcome of the calcium-lowering drugs given was not satisfactory. This complication was critical to the life of the patient, and the patient was found to have indications requiring blood purification. A catheter was placed in the right femoral vein for blood purification using continuous venous hemodiafiltration (CVVHDF) with 4% citric acid anticoagulation at a speed of 220 mL/hour, dialysate 2,000 mL/hour, post-replacement 1,000 mL/hour, 5% sodium bicarbonate 100 mL/hour, with balance of incoming and outgoing. The replacement fluid configuration did not consist of calcium ions and had physiological salt of 2,250 mL, water for injection of 500 mL, 5% glucose of 250 mL, 25% magnesium sulfate of 2.4 mL, and 10% potassium chloride of 10 mL. After 2 hours on the machine, the patient's serum Ca^{2+} was rechecked, which was found to be significantly lower than before (2.34 mmol/L). On the third day after surgery, her serum Ca^{2+} had returned to normal (2.01 mmol/L), while amylase showed a continuous downward trend. The right femoral vein catheter is removed from the right femoral vein, and ulinastatin was continued to act against pancreatitis exudation. The patient's condition improved on the fourth day following surgery, and she was transferred to a general obstetric ward for conventional treatment. Prior to discharge, a repeat abdominal CT showed that the pancreatic edema had improved, and the patient was discharged 15 days after delivery. The newborn was discharged after 30 days and completed neonatal screening. The patient un-

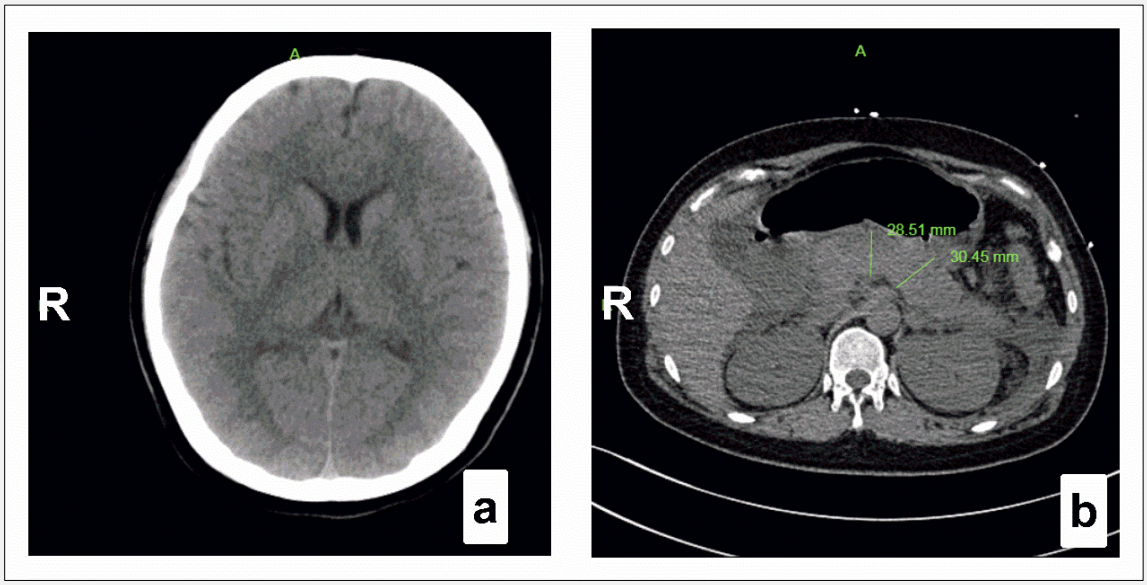

Figure 1. a) Brain CT scan results in cross section. b) CT scan results of abdominal pancreas in cross section.

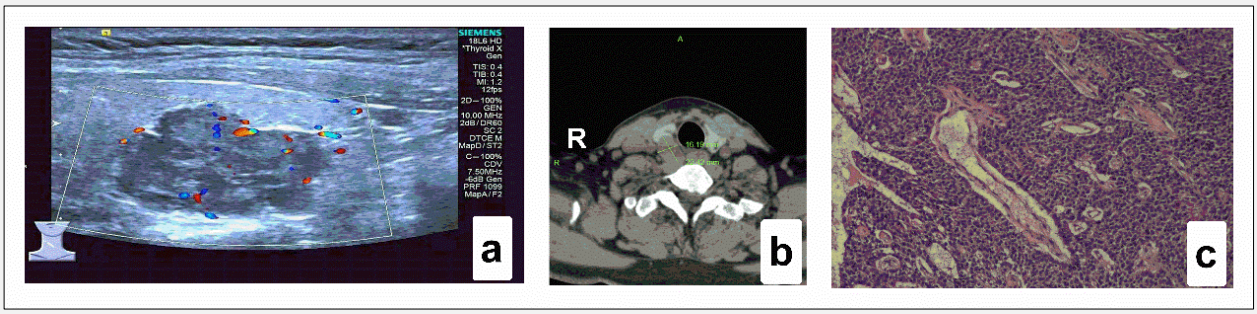

Figure 2. a) Parathyroid B-ultrasound results. b) Parathyroid CT scan results in cross section. c) Postoperative hematoxylin and eosin (H&E) stained sections of parathyroid tissue (x 100).

derwent surgical treatment in the thyroid surgery department at our hospital two months later. The postoperative pathology showed a parathyroid adenoma (Figure 2c).

DISCUSSION

This study introduced a patient suffering from eclampsia at 33 weeks gestation (gravida 2, para 1) who had severe hypercalcemia and acute pancreatitis following delivery. It was preliminarily confirmed that the cause was primary hyperparathyroidism that had a certain relationship with eclampsia. PHPT is a relatively common endocrine disease, whose main manifestations are elevated serum calcium and normal or elevated parathyroid

hormone (PTH). Although this standard can be used for the diagnosis of PHPT during pregnancy, physiological changes during pregnancy can make the serum calcium level drop to cover PHPT [7]. When the serum ionic calcium level increases during pregnancy, or when the serum albumin is adjusted to normal, the serum calcium level increases along with a rise in serum PTH. After other causes of hypercalcemia are excluded, a diagnosis of PHPT can be established [8]. During pregnancy, certain radiological techniques that check for parathyroid adenomas and hyperplasia are not recommended. Accordingly, 99mTc radionuclide imaging is the most sensitive technique that has been avoided due to its risk of radiation. Therefore, neck ultrasound is considered to be the first-line examination used during pregnancy [9]. As reported in this article, the diagnosis of PHPT was made after delivery, and in light of the severity of the patient's presentation as well as the age of the patient, it was important to rule out hereditary syndromes. PHPT can cause serious maternal and pediatric complications. The more common maternal complications include: hyperemesis gravidarum, kidney stones, skeletal lesions, as well as increased blood pressure, and insulin resistance. When the serum calcium level is extremely high, it can also cause pancreatic inflammation. When a pregnancy is complicated by PHPT, the incidence of pancreatitis can reach as high as 7% to 13%, which may even lead to a hypercalcemic crisis. Severe patients can be subject to hematuria, coma, and even death. As also put forward by Dale et al. [10], our patient also developed pancreatitis, which may have been caused by hypercalcemia due to hyperparathyroidism. Contrary to Dale et al., however, the patient in this study was diagnosed with pancreatitis after delivery. She had not been diagnosed with pancreatitis before, however, she received adequate supportive treatment.

Eclampsia is a hypertensive disease that is unique to multiple systems during pregnancy [11]. Endothelial cell activation and dysfunction are considered as the core pathological features of pre-eclampsia. Moreover, vasospasm is a key pathological feature, and hypertension is one of its basic diagnostic criteria. Women with PHPT have an increased risk of preeclampsia. The link between the two diseases appears to be the interaction of PTH with the renin-aldosterone system, sympathetic nervous system, and vascular endothelium. Eclampsia in PHPT patients can lead to serious complications. As reported in this article, uncontrolled hypertension and frequent seizures allowed us to exclude other pathologies, such as intracerebral hemorrhage and seizures. Some of the severe symptoms reported by Dale et al. occurred prior to delivery. In this study, however, the patient's clinical deterioration occurred after delivery, with complications such as confusion, hypercalcemia, and acute edematous pancreatitis.

When pregnant patients with PHPT are not effectively treated, 80% of patients will have fetal or neonatal complications, including fetal growth restriction, low birth weight, premature delivery, intrauterine death, stillbirth, neonatal hand-foot twitching, and thyroid hypoparathyroidism, while 27% - 31% of complications will cause neonatal death [12]. The newborn's birth weight in this study was 1,280 grams, and when combined with the child's gestational age, intrauterine growth retardation (IUGR) was considered. Due to the low incidence of PHPT in pregnancy, most existing research studies are limited to case reports, and recommendations for treatment are not included in the recent PHPT treatment guidelines. Therefore, the treatment of PHPT during pregnancy should be individually designed according to the patient's symptoms, severity of hypercalcemia, size of gestational age, and risk/benefit ratio. In addition, having a multidisciplinary team that includes the Endocrinology Department is very important. Kelly found that the incidence of fetal complications in drug-treated pregnancy patients with PHPT was 53%, while the rate of fetal complications was 12.5% in patients undergoing surgical treatment [13,14]. In this case, the efficacy of drug therapy in lowering calcium was found to be poor. In addition, there were complications that endangered the patient's life, for which timely hemodialysis treatment is effective. Due to the severity of hypercalcemia and clinical instability, the patient was treated with zoledronic acid and other calcium-lowering drugs. The patient then underwent surgical treatment two months postpartum. The pathological diagnosis following surgery was confirmed to be a single parathyroid adenoma. Meanwhile, the patient's clinical history was noted to differ from that demonstrated by Ghaznavi et al. [15]. Here, we reported a previously healthy woman who had no personal or family clinical history before the serious event that led to the diagnosis.

The clinical symptoms of PHPT during pregnancy are non-specific and are difficult to identify. Moreover, they are often hidden due to physiological changes during pregnancy, thus making diagnosis difficult. When pregnant women suffer from any clinical manifestations related to hypercalcemia, a relevant examination to investigate PHPT is necessary. At the same time, it is very important to closely monitor the status of the mother and fetus in order to prevent deterioration and hypercalcemic crisis.

Source of Funds:
The study was supported School Funded Projects of Anhui Medical University (No. 2021xkj094).

Informed Consent:
Written informed consent was obtained from the patient and her immediate family.

Declaration of Interest:
The authors have disclosed no conflicts of interest.

References:

1. Dawood NB, Yan KL, Shieh A, Livhits MJ, Yeh MW, Leung AM. Normocalcaemic primary hyperparathyroidism: An update on diagnostic and management challenges. Clin Endocrinol (Oxf) 2020;93(5):519-27. (PMID: 32803770)

2. Walker MD, Silverberg SJ. Primary hyperparathyroidism. Nat Rev Endocrinol 2018;14(2):115-25. (PMID: 28885621)

3. Carella MJ, Gossain VV. Hyperparathyroidism and pregnancy: case report and review. J Gen Intern Med 1992;7(4):448-53. (PMID: 1506954)

4. Behrens M, Boyle S, Fingeret AL. Evaluation for Primary Hyperparathyroidism in Patients Who Present With Nephrolithiasis. J Surg Res 2021;2021(257):79-84. (PMID: 32818787)

5. Kamenicky P, Lecoq AL, Chanson P. Primary hyperparathyroidism in pregnancy. Ann Endocrinol (Paris) 2016;77(2):169-71. (PMID: 27157105)

6. Hultin H, Hellman P, Lundgren E, et al. Association of parathyroid adenoma and pregnancy with preeclampsia. J Clin Endocrinol Metab 2009;94(9):3394-9. (PMID: 19531594)

7. Cusano NE, Cipriani C, Bilezikian JP. Management of normocalcemic primary hyperparathyroidism. Best Pract Res Clin Endocrinol Metab 2018;32(6):837-45. (PMID: 30665550)

8. Ong GS, Walsh JP, Stuckey BG, et al. The importance of measuring ionized calcium in characterizing calcium status and diagnosing primary hyperparathyroidism. J Clin Endocrinol Metab 2012; 97(9):3138-45. (PMID: 22745247)

9. Soto GD, Halperin I, Squarcia M, Lomena F, Domingo MP. Update in thyroid imaging. The expanding world of thyroid imaging and its translation to clinical practice. Hormones (Athens) 2010; 9(4):287-98. (PMID: 21112859)

10. Dale AG, Holbrook BD, Sobel L, Rappaport VJ. Hyperparathyroidism in Pregnancy Leading to Pancreatitis and Preeclampsia with Severe Features. Case Rep Obstet Gynecol 2017;2017(4): 6061313. (PMID: 28487796)

11. Xu HL, Cui J, Jia R, Liu X, Wang YJ. Relationship between onset of eclampsia and AGTR1 gene polymorphisms. Eur Rev Med Pharmacol Sci 2020;24(24):12638-44. (PMID: 33378010)

12. Dochez V, Ducarme G. Primary hyperparathyroidism during pregnancy. Arch Gynecol Obstet 2015;291(2):259-63. (PMID: 25367603)

13. Kelly TR. Primary hyperparathyroidism during pregnancy. Surgery 1991;110(6):1028-34. (PMID: 1745971**)**

14. McMullen TP, Learoyd DL, Williams DC, Sywak MS, Sidhu SB, Delbridge LW. Hyperparathyroidism in pregnancy: options for localization and surgical therapy. World J Surg 2010;34(8):1811-6. (PMID: 20386905)

15. Ghaznavi SA, Saad NM, Donovan LE. The Biochemical Profile of Familial Hypocalciuric Hypercalcemia and Primary Hyperparathyroidism during Pregnancy and Lactation: Two Case Reports and Review of the Literature. Case Rep Endocrinol 2016; 2016(11):2725486. (PMID: 27957351)