

## Case Report

# Acute pancreatitis and preeclampsia induced by parathyroid adenoma in pregnancy: a case report and literature review

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**Abstract:** Primary hyperparathyroidism (PHP) during pregnancy is very rare, and the complications are life threatening and difficult to address. Thus, early diagnosis and appropriate treatment are critical for this disease. We describe a single case of PHP during third trimester pregnancy, which was also combined with hypertension. The patient developed preeclampsia and went into a hypercalcemic crisis; an ultrasound examination found no lesion in the parathyroid gland, and a Cesarean delivery was performed at 31 weeks. After delivery, acute pancreatitis occurred. Subsequently, a second ultrasound and an MRI examination found a mass behind the lower-right thyroid gland, both suggesting parathyroid adenoma. A successful parathyroidectomy was conducted, and the patient was finally cured. Diagnosis of PHP during pregnancy is challenging for the physician. Untreated hypercalcemia can be life-threatening and can induce the onset of preeclampsia, which is a major cause of maternal and fetal mortality. Acute pancreatitis is the third most common complication of PHP, after nephrolithiasis and bone disease, and causes a severe outcome if not treated promptly. Surgery is the gold standard of treatment for PHP during pregnancy, and a parathyroidectomy during the second trimester of pregnancy is considered safe and effective.

**Keywords:** Primary hyperparathyroidism, hypercalcemia, hypertension, acute pancreatitis, pregnancy

## Introduction

Primary hyperparathyroidism (PHP) during pregnancy is very rare, and the complications are life threatening and difficult to address. Thus, early diagnosis and appropriate treatment are critical for this disease. Here, we describe a single case of PHP during third trimester pregnancy, which was also combined with preeclampsia.

## Patient presentation

A 33-year-old primigravid woman complained of headache, dizziness, nausea, vomiting and irritability at 31 weeks of gestation. On examination, her supine blood pressure was 165/101 mmHg, and it was recommended that she receive labetalol for blood pressure control and be admitted immediately to the hospital for further examination. Laboratory tests showed hypercalcemia with a serum calcium level of

3.79 mmol/L. After consulting the endocrinologist, hyperparathyroidism was suspected, which was confirmed by an elevated parathyroid hormone (PTH, 18.7 pmol/L) level, but a Doppler scan found no abnormality in her neck. She was diagnosed with pregnancy-associated hypertension crisis, hyperparathyroidism and hypercalcemic crisis. The patient had no previous history of inherited hyperparathyroidism or other endocrine conditions, kidney stones, ostealgia or neck irradiation.

Due to the severity of her situation, a low calcium diet and diuretics combined with fluid supply were recommended, and labetalol was also advised to control hypertension. Meanwhile, she was also treated with dexamethasone to promote fetal lung maturity. An emergency Cesarean delivery was performed at 31 weeks of pregnancy, and she delivered a live-born baby girl weighing 1.3 kg, with Apgar scores of 10 at both 1 and 5 minutes. The baby was

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**Figure 1.** Ultrasound scan of the thyroid and parathyroid demonstrating findings consistent with a parathyroid adenoma.



**Figure 2.** MRI scans indicated a well-defined T2 hyperintense lesion on the lower-right side suggestive of parathyroid adenoma.

hypercalcemic with a calcium level of 3.14 mmol/L on the same day of delivery and a PTH level of 62.5 pmol/L, with no seizure or tetany. After 3 days, the calcium level decreased to normal without any treatment.

After surgery, the patient complained of headache and confusion; her blood pressure was 160-171/105-116 mmHg, and her calcium level was 3.28 mmol/L. As a precaution, in case of hypertension and hypercalcemic cri-

sis, the patient was transferred to the intensive care unit (ICU). In the ICU, urapidil was used intravenously to control blood pressure, and she was managed with calcitonin combined with a low calcium diet, intravenous fluid infusion and diuretic therapy. A sestamibi scan of the neck was performed, but parathyroid imaging was negative. The patient complained of upper abdominal pain accompanied by fever and significant elevation of white blood cells (WBC,  $15.24 \times 10^9/L$ ), hemodiastase (1,235 U/L) and lipase (875 U/L). The abdominal CT scan showed a swollen pancreas with normal density, and small patchy effusion shadows could be found around the pancreas.

Due to the onset of acute pancreatitis, octreotide and antibiotics were administered, and hemodialysis was also performed to correct hypercalcemia. The calcemic level was significantly decreased after 3 days of dialysis.

After recovery, another neck ultrasound showed a well-defined mass, hypoechoic to the thyroid tissue with a homogenous echo behind the lower-right thyroid gland, measuring 11 mm×18 mm×17 mm with few vascular structures in the lower part (**Figure 1**). MRI also showed a well-defined T2 hyperintense lesion in the lower-right side measuring 13×8 mm, suggestive of parathyroid adenoma (**Figure 2**). Finally, the patient underwent surgical removal of the parathyroid gland. The removed gland measured 2 cm×1 cm, and the pathological report noted adenoma. After the surgery, the patient was normocalcemic. Her PTH level decreased significantly ( $<0.32$  pmol/L), and she was discharged in good general condition on the fifth day after surgery.

## Discussion

PHP is an uncommon disease with a prevalence of 0.15% in the general population. A solitary parathyroid adenoma is the most common cause of PHP in the general population and accounts for approximately 80-85% of cases. The remaining 15-20% of cases can be attributed to diffuse hyperplasia (10-12%),

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multiple adenomas (3%) or carcinomas (2%) [1]. PHP is the third most common endocrine disorder, after diabetes and thyroid disease, and women are affected with PHP three times more often than men [2]. The exact incidence of PHP during pregnancy is unknown, and approximately only 150 cases have been reported in the literature. Due to the severe complications induced by PHP, diagnosis during pregnancy is very important for clinicians.

Diagnosis of PHP is challenging because most PHP patients are asymptomatic. The presentation of hypercalcemia during pregnancy related to PHP is variable and ranges from asymptomatic cases to symptoms such as nausea, vomiting, anorexia, weakness, fatigue and neurological/psychiatric manifestations [3]. A diagnosis of PHP during pregnancy should be considered with the simultaneous findings of an elevated total calcium level ( $>2.37$  mmol/L) or an ionized calcium level, hypophosphatemia ( $<0.8$  mmol/L) and an elevated serum PTH level in the absence of other causes of hypercalcemia [4]. An ultrasound scan of the neck is the first choice during pregnancy for localization of parathyroid adenomas, and this method has a sensitivity of 69% and a specificity of 94% [5]. CT and sestamibi scintigraphy for the detection of parathyroid adenomas are contraindicated during pregnancy due to the potential risks of ionizing radiation to the fetus. In our case, the patient suffered from hypertension and hypercalcemia, which was suspected to be caused by PHP. However, the first ultrasound did not indicate swelling of the parathyroid, which made determining appropriate treatment difficult. After the delivery, the sestamibi scan of the neck was also negative, showing no indication of the location of the problem. We performed another ultrasound scan and MRI examination, which found the parathyroid adenoma behind the lower-right side thyroid lobe, and this finding made it possible to perform the parathyroidectomy. The location of an enlarged parathyroid is crucial for appropriate treatment, and repeated ultrasound examinations, combined with sestamibi scintigraphy and MRI, if necessary, are imperative. Assessment of PTH concentrations in different branches of thyroid veins via a vascular intervention method can also help identify the lesion.

PHP has been reported to lead to maternal complications in 2/3 of cases. Nephrolithiasis

(24-36%) is the most common maternal complication followed by bone disease and pancreatitis (7-13%). Pancreatitis is considered an ominous sign of disease severity and can occur simultaneously with a hypercalcemic crisis. Other maternal complications include gravidarum, preeclampsia, tremors, fractures, depression, blurred vision, uremia, seizures and coma [3]. Preeclampsia is a syndrome characterized by the onset of hypertension and proteinuria after 20 weeks of gestation and is a major cause of maternal, fetal and neonatal morbidity and mortality [6, 7]. Abnormal development of the placenta, immunologic factors, increased sensitivity to angiotensin II, systemic endothelial dysfunction, inflammation and infection play a role in the development of preeclampsia. Hypertension is frequently observed in patients with PHP. The effects of PTH on stimulating the activity of the renin aldosterone system, hyperinsulinemia on stimulating the secretion of cortisone and aldosterone, endothelial dysfunction on increasing the sympathetic drive, and direct effects on vascular smooth muscle cells [8] are the mechanisms that have been proposed to explain the relationship between hyperparathyroidism and hypertension. In our case, mental confusion and preeclampsia were likely induced by hypercalcemia, and hypertension was not well controlled, even after delivery, until a parathyroidectomy was performed.

It has been reported that the fetal complication rate is as high as 80% in mothers with PHP who did not receive appropriate treatment, and the most serious fetal complications include neonatal tetany, still birth and miscarriage [9], with tetany being the primary cause of neonatal morbidity. Tetany is mainly due to suppressed parathyroid gland development in infants whose mothers had untreated PHP during pregnancy.

The third international workshop published revised evidence-based guidelines on the management of patients with PHP in 2009 [10]. Unfortunately, due to the rarity of PHP during pregnancy, these guidelines do not include any official recommendations for pregnant women. However, management recommendations can be found elsewhere in the published literature. Asymptomatic patients who have mild hyper-

calcemia (<2.74 mmol/L) can be reasonably managed with conservative medical procedures, such as oral hydration, low calcium intake and close fetal surveillance [9]. Calcitonin is also administered to PHP patients and has a category C rating. Calcitonin is somewhat limited in effectiveness, due to tachyphylaxis. Cinacalcet has also been used along with calcitonin and has demonstrated a highly effective reduction in PTH levels. Cinacalcet has a category C rating, but studies evaluating its effects on mothers and fetuses/neonates are still lacking. A minimally invasive parathyroidectomy during the second trimester is the therapeutic gold standard and most definitive treatment of PHP during pregnancy. First-trimester surgery is avoided due to incomplete organogenesis, and third-trimester surgery has been discouraged because it is associated with a higher risk of preterm labor. Because increasing evidence supports higher morbidity and mortality associated with calcium levels >2.84 mmol/L, surgical intervention is recommended for patients with levels >2.74 mmol/L, particularly in patients with prior pregnancy loss. In our case, the patient underwent a parathyroidectomy after delivery at 31 weeks, which is still thought to be safe for both mother and fetus.

In conclusion, PHP is a rare endocrine disorder during pregnancy, and most PHP patients are asymptomatic, which makes the diagnosis of this disease difficult. PHP can be associated with significant maternal and fetal morbidity and mortality, if not recognized and managed appropriately. Untreated hypercalcemia can be life-threatening and can induce the onset of preeclampsia, which is a major cause of maternal and fetal morbidity. Acute pancreatitis is the third most common complication of PHP, after nephrolithiasis and bone disease, and can result in a severe outcome if not treated promptly. Surgery is the gold standard treatment for PHP during pregnancy, and a parathyroidectomy performed during the second trimester is recommended as safe and effective.

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### Disclosure of conflict of interest

None.

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