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Case report

PRIMARY HYPERPARATHYROIDISM IN PREGNANCY: A CASE REPORT HIGHLIGHTING UNCOMMON COMPLICATION

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Abstract

Primary hyperparathyroidism (PHPT) is characterized by elevated levels of calcium and parathyroid hormone (PTH). However, the interpretation of diagnostic tests, such as serum calcium and PTH levels, is complex in pregnant women. The aim of this report is to present a case of PHTP in a pregnant adolescent, with a special emphasis on an uncommon complication, as well as diagnostic and treatment strategies.

A 17-year-old pregnant female presented with hyperemesis gravidarum and neurological symptoms, leading to the diagnosis of cerebral venous thrombosis. Further investigations revealed hypercalcemia and persistently elevated PTH levels, consistent with PHPT. After localization studies, the patient underwent an emergency parathyroidectomy with a diagnosis of parathyroid adenoma. During follow-up, intrauterine growth restriction and severe preeclampsia developed, necessitating an emergency cesarean section. Both the mother and neonate had favorable outcomes.

PHPT is an infrequent condition in the pregnant population, and its diagnosis can be challenging due to the overlap of symptoms with normal physiological changes during pregnancy. The occurrence of uncommon complications, such as thrombotic phenomena, highlights the need for a comprehensive approach to ensure early detection and management. In most cases, parathyroidectomy is the treatment of choice.

Key words: primary hyperparathyroidism, pregnancy, hypercalcemia, parathyroid adenoma, cerebral venous thrombosis, preeclampsia

Resumen

Hiperparatiroidismo primario en el embarazo: reporte de caso destacando una complicación infrecuente

El hiperparatiroidismo primario (HPTP) se caracteriza por niveles elevados de calcio y hormona paratiroidea (PTH). Sin embargo, la interpretación de pruebas diagnósticas, como los niveles de calcio sérico y PTH, es compleja en mujeres embarazadas. El objetivo de este reporte es presentar un caso de HPTP en una adolescente embarazada, con especial hincapié en una complicación infrecuente, así como en las estrategias diagnósticas y de tratamiento.

Una mujer embarazada de 17 años presentó hiperémesis gravídica y síntomas neurológicos, lo que llevó al diagnóstico de trombosis venosa cerebral. Posteriores investigaciones revelaron hipercalcemia y niveles persistentemente elevados de PTH, consistentes con HPTP. Tras la realización de estudios de localización, la paciente fue sometida a una paratiroidectomía de emergencia con diagnóstico de adenoma de paratiroides. Durante el seguimiento, se desarrolló restricción

del crecimiento intrauterino y preeclampsia grave, lo que resultó en la necesidad de realizar una cesárea de emergencia. Tanto la madre como el neonato evolucionaron favorablemente.

El HPTP es una condición infrecuente en la población embarazada y su diagnóstico puede ser desafiante por la superposición de síntomas con los cambios fisiológicos normales del embarazo. La aparición de complicaciones infrecuentes, como fenómenos trombóticos, resalta la necesidad de un abordaje integral para garantizar la detección y el manejo temprano. En la mayoría de los casos, la paratiroidectomía es el tratamiento de elección.

Palabras clave: hiperparatiroidismo primario, embarazo, hipercalcemia, adenoma de paratiroides, trombosis venosa cerebral, preeclampsia

Primary hyperparathyroidism (PHPT) is characterized by elevated levels of calcium and parathyroid hormone (PTH)[1]. It affects approximately 0.3% of the general population, with women experiencing twice the incidence, and both pregnant and nonpregnant women having a similar frequency[2]. Nonspecific clinical manifestations and changes in calcium metabolism that occur during pregnancy can complicate the diagnosis of PHPT[3].

Studies suggest a correlation between higher calcium levels and increased risks of maternal, fetal, and neonatal complications[4,5]. Mild cases of PHPT can be managed conservatively, but in cases of severe or symptomatic hypercalcemia, parathyroidectomy is the treatment of choice[3].

The aim of this presentation is to highlight an unusual case of PHPT in a pregnant woman, with a particular emphasis on the complications, diagnostic methodologies, and therapeutic interventions implemented.

Clinical case

Patient, a 17-year-old female was admitted to the hospital with a history of 9-week amenorrhea and intolerance to fluids and solids lasting over a week. Pregnancy at 9.1 weeks was confirmed by obstetric ultrasound (US), and the condition was interpreted as gravidarum hyperemesis. Treatment was initiated with fluid replacement, vitamin B supplementation, and antiemetics.

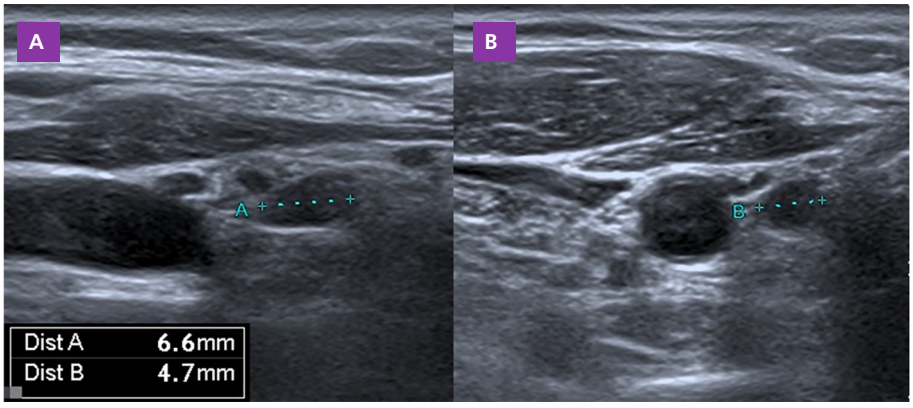
After 24 hours, the patient developed severe headache, photophobia, muscular weakness, difficulty walking, and right sided faciobrachiocrural hemiparesis accompanied by ipsilateral hemihypoesthesia. An urgent computed tomography of the brain revealed acute cerebral venous thrombosis in the superior sagittal sinus and left transverse sinus. A cerebral angiography was performed, confirming the diagnosis of dural sinus thrombosis (longitudinal, transverse, and left sigmoid). Thrombophilia studies yielded normal results. Concurrently, serum calcium level was found to be 10.7 mg/dl and 25(OH)D was 3 ng/ml (Table 1). Biochemical parameters of renal function were within normal range. The patient was discharged with a prescription of enoxaparin and vitamin D_3.

During follow-up, total serum calcium level was found to be 13.4 mg/dl, ionized calcium 6.6 mg/dl, PTH 59.8 pg/ml, and urinary calcium excretion 618 mg/day (Table 1). These results confirmed the diagnosis of PHPT in the woman at 19.1 weeks of gestation. The patient was readmitted for the establishment to treat hypercalcemia (Table 1). Upon discharge, a parathyroid US was performed, revealing a 6.6 mm hypoechoic solid nodule located behind the lower pole of the right thyroid lobe, suggestive of a parathyroid adenoma (Fig. 1).

Table 1 | Biochemical characteristics of the patient during the evolution

	Initial	At diagnosis	Before surgery	After surgery
Parathyroid hormone (15-65 pg/ml)		59.8	68.2	15.95
Corrected calcium (8.5-10.5 mg/dl)	10.7	13.4	11.2	9.46
Ionized calcium (4.5-5.2 mg/dl)		6.6	6.31	5.27
Phosphorus (2.8-4.5 mg/dl)		2.7	2.50	2.31- 3.3
24-hour urinary calcium (80-250 mg/day)		618	322	
24-hour urinary phosphate (40-1300 mg/day)		2360	536	
Vitamin D (≥30 ng/ml)	3	17	21	
Creatinine (0.5-0.9 mg/dl)			0.6	0.8

Figure 1 | Ultrasonographic findings of parathyroid adenoma. The patient's ultrasound scan revealed a 6.6-mm adenoma of the lower portion of the right parathyroid gland. A: Sagittal orientation. B: Transverse orientation



At 24 weeks of pregnancy, an obstetric US revealed a fetal weight of 511 grams, estimated gestational age of 21.5 weeks, and increased resistance in the uterine arteries. These findings indicated intrauterine growth restriction (IUGR). Furthermore, ventricular extrasystoles were observed in the maternal electrocardiogram.

A multidisciplinary decision was made to perform surgical intervention for PHPT, considering the persistent hypercalcemia and hypercalciuria alongside the presence of IUGR. A parathyroidectomy was performed on the lower right parathyroid gland. Corrected calcium levels, accounting for albumin, were recorded at 9.3 mg/dl (Table 1). Obstetric evaluation demonstrated preserved fetal well-being, and the patient was discharged on the seventh day. The histopathological analysis revealed a parathyroid adenoma with a maximum diameter of 9 mm and no signs of malignancy.

During the follow-up period, the patient developed severe hypertension, proteinuria of 7 grams in a 24-hour period, and IUGR, suggestive of severe preeclampsia. At 33.1 weeks of gestation, the decision was made to admit the patient for antihypertensive treatment and expedite delivery. An emergency cesarean section was performed after discontinuing enoxaparin, resulting in the birth of a female neonate. The neonate had a gestational age of 33 weeks, and birth weight of 1320 grams. Apgar scores of 8 at one minute and 9 at five minutes were obtained to assess the neonate's condition.

This publication was approved by the Ethics Committee, and written informed consent was obtained from the patient.

Discussion

PHPT is a common cause of hypercalcemia and is characterized by elevated levels of calcium and PTH[1]. In this case, we present an occurrence of PHPT in a pregnant adolescent, elucidating the related complications, the employed diagnostic methodology, and the established treatment.

It is well-established that women, both pregnant and nonpregnant, have a higher incidence of PHPT compared to men[2]. The hormonal and metabolic changes during pregnancy can complicate the diagnosis, as the symptoms of PHPT may overlap with those commonly seen in pregnancy[3]. During pregnancy, total calcium concentrations may appear falsely lower and PTH may be physiologically suppressed. PTH levels can decrease because of the physiological rise in parathyroid hormone-related protein. Its levels begin to increase as early as 3–13 weeks into gestation and continue to peak in the third trimester, which can lead to the suppression of PTH levels[3]. The combination of elevated ionized or albumin-corrected calcium associated with detectable PTH is indicative of PHPT in most cases[6]. The diagnosis of PHPT in our patient was confirmed by elevated calcium levels and normal/high PTH levels.

Approximately 10% of cases of PHPT are attributed to hereditary syndromes such as multiple endocrine neoplasia, familial hypocalciuric hypercalcemia, hyperparathyroidism jaw tumor, and familial isolated PHTP[7]. The remaining 90% of cases are sporadic, commonly caused by parathyroid adenomas. Due to the earlier age of onset of familial parathyroid disorders compared to

sporadic disease, genetic testing should be considered in pregnant women with PHPT[7]. In our case, we did not have the availability to carry out genetic testing, but it will be a matter to be considered in the future. This approach will allow us to assess the necessity of organ-specific examinations, including those involving the pituitary gland, thyroid, adrenal glands, pancreas, and other relevant structures.

The optimal method for localizing parathyroid adenomas in PHPT during pregnancy remains a topic of debate. US has a sensitivity of 69% and specificity of 94% for diagnosing and localizing parathyroid adenomas[8]. Sestamibi scanning, which has a sensitivity of 80% to 99% for single adenoma identification, is not recommended during pregnancy due to the potential placental transfer of 99-Tm-sestamibi[9]. Given the limitations of imaging modalities during pregnancy, a bilateral surgical approach may be required to locate all four parathyroid glands[6,10]. Intraoperative PTH monitoring, validated in non-pregnant individuals, can be employed to confirm successful excision of the glands[3].

The clinical presentation and the occurrence of maternal, fetal, and neonatal complications in pregnant women with PHPT are influenced by the level of hypercalcemia. Numerous studies have demonstrated an increased risk of adverse outcomes, including preeclampsia, IUGR, maternal hypertension, and other complications, in pregnant women with PHPT[4,5,11]. Nephrolithiasis is commonly observed in symptomatic patients with PHPT during pregnancy. Fetal complications associated include premature birth, IUGR, low birth weight, neonatal hypocalcemia, and tetany due to the suppression of fetal parathyroid tissue[3-5]. Our patient developed preeclampsia following the resolution and remission of the disease of PHTP. This finding should not be surprising, as it has been demonstrated that a history of parathyroid adenoma, even up to 5 years before delivery, is associated with an increased risk of preeclampsia[11]. These complications underscore the importance of multidisciplinary management in pregnant patients with PHPT, as close monitoring and timely intervention are essential for optimizing outcomes.

In our case, the patient presented with venous sinus thrombosis, which added further complexity to the management. Thrombophilia studies yielded normal results, indicating that the thrombosis may be associated with hypercalcemia. Several potential mechanisms have been proposed to explain the pathophysiological link between calcium and thrombosis. Calcium can induce vasoconstriction by activating vascular smooth muscle, triggering platelet aggregation, and activating various clotting factors[12]. Increases in platelet count, elevated factor FVII and FX activities, elevated D-dimer, elevated levels of tissue plasminogen activator inhibitor-1 (PAI-1) and tissue plasminogen activator, and decreased levels of factor pathway inhibitor were observed in PHTP[13]. Additionally, it has been demonstrated that there is a correlation between elevated PAI-1 and PTH levels in PHPT patients[14]. However, the possibility that PHPT may synergically promote thrombosis when interacting with other prothrombotic factors such as mutations or autoimmune cannot be excluded.

The management of PHPT during pregnancy should be based on gestational age, severity of hypercalcemia, and risk-benefit balance. In cases of symptomatic hypercalcemia or when complications are present, surgery is the preferred treatment option[3,8]. Research has shown that parathyroidectomy during pregnancy in women with gestational HPT resulted in a significantly lower neonatal complication rate compared to medical therapy[15]. The optimal timing for surgery is in the second trimester, especially if albumin-adjusted calcium is above >11.42 mg/dl and/or above >1 mg/dl upper limit of normal, and/or ionized calcium is above >5.81 mg/dl, as in the first trimester fetal organogenesis takes part and in the third trimester the risk for preterm labor increases[3]. Close monitoring of calcium levels and a conservative treatment approach may be appropriate for mild to moderate hypercalcemia (serum calcium <11 mg/dl), but if maternal-fetal complications occur or conservative medical therapy fails, urgent parathyroidectomy is recommended regardless of fetal gestational age[15]. However, some studies suggest that mild hypercalcemia may not exclude the possibility of severe complications[4, 5].

In conclusion, this case underscores the challenges in diagnosing and managing PHPT in pregnancy. Early recognition, appropriate diagnostic evaluation, and tailored management, including parathyroidectomy when indicated, are crucial to mitigate the risks associated with PHPT in pregnancy and optimize maternal and fetal outcomes.

Conflict of interest: None to declare

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