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Third Trimester Parathyroidectomy in Gestational Primary Hyperparathyroidism: A Case Report

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Abstract Primary hyperparathyroidism (PHPT) is characterized by the overproduction of parathyroid hormone (PTH) due to parathyroid gland hyperplasia, adenoma, or carcinoma, resulting in hypercalcemia and raised or inappropriately normal PTH levels. Primary hyperparathyroidism is rare in pregnancy, with a reported incidence of one percent. There is a direct relationship between the degree of severity of hypercalcemia and miscarriage risk, with higher rates being reported in those patients, whose serum calcium levels are greater than 11.4 mg/dL (2.85mmol/L). After taking written informed consent, we report a case of 32 years old female in the third trimester of pregnancy, who presented with recurrent symptomatic hypercalcemic episodes. A successful parathyroidectomy was performed during the third trimester of pregnancy. The patient responded dramatically with no subsequent post-operative feto-maternal complications and normal post-operative serum calcium levels. During pregnancy, the diagnosis of primary hyperparathyroidism can be difficult due to physiological changes of pregnancy. Besides this, a precise radiological diagnosis of the overactive parathyroid gland is not possible due to the risk of radiation injury to the fetus. This can lead to persistent hypercalcemia associated with numerous dreadful feto-maternal complications. In literature, there is conflicting data regarding the management of gestational hyperparathyroidism, especially during the third trimester of pregnancy. From this case, it is concluded that in a patient with recurrent symptomatic hypercalcemic episodes, even during the third trimester of pregnancy, emergency parathyroidectomy can be considered regardless of gestational age.

Keywords: *hyperparathyroidism, pregnancy, parathyroidectomy, hypercalcemia, miscarriages*

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1. Introduction

Primary hyperparathyroidism (PHPT) is characterized by the overproduction of parathyroid hormone(PTH) due to parathyroid gland hyperplasia, adenoma, or carcinoma, which results in hypercalcemia and raised or inappropriately normal PTH levels [1]. Clinical data for the treatment of PHPT in pregnancy is limited; however, most studies have determined the specific treatment options considering the severity of the disease, which is determined by the serum calcium levels, symptoms at the time of presentation, and gestational age [2]. Primary gestational hyperparathyroidism can be associated with falsely low serum calcium levels, contributing to diagnostic dilemma.

Regarding conservative management of gestational primary hyperparathyroidism, hydration with or without forced diuresis and restriction of calcium and vitamin D intake are recommended. Clinical use of commonly prescribed drugs like cinacalcet [3], calcitonin [4], and bisphosphonates have not been validated in pregnancy due to limited safety data. Therefore, parathyroidectomy might be considered as a definitive treatment modality. For parathyroidectomy, the second trimester of pregnancy is recommended to be the safest period [2,5]. However, there is conflicting data regarding third-trimester parathyroidectomy. We report a case of successfully treated gestational primary hyperparathyroidism with parathyroidectomy done in the third trimester.

2. Case Presentation

32 years old lady (G_3P_2), with gestational amenorrhea of 24 weeks and unremarkable obstetric visits, presented in the emergency department with left-sided loin pain and increased urinary frequency. Her past medical history was suggestive of bilateral renal stones, hypercalcemia, and previous two uneventful pregnancies. Laboratory evaluation revealed serum calcium of 13.9 mg/dL and serum phosphorus of 2.3 mg/dL. Ultrasound showed four calculi at the lower pole of the right kidney with mild pelvicalyceal fullness, left-sided grade 2 renal parenchymal echogenicity along with moderate to gross hydronephroureter, and a 5.6 mm calculus at the left distal ureter. She was managed with left percutaneous nephrolithotomy (PCNL) and intravenous hydration. A tailored workup for hypercalcemia showed

decreased vitamin D levels of 14 ng/mL, no paraproteins in serum and urine, and normal renal function.

On her follow-up visit, at 26 weeks, serum calcium was persistently high at 12.3 mg/dL. Furthermore, her serum phosphorus was 1.4 mg/dL, serum albumin 3.6 mg/dL and intact PTH was raised to 250 pg/mL (reference range 15-65 pg/mL). These findings were strongly suggestive of primary hyperparathyroidism; therefore, obstetrician, ENT, and endocrinology teams were taken on board. Her ultrasound neck revealed a calcified nodule in the right lobe of the thyroid gland, but there was no sonographic evidence of parathyroid adenoma or hyperplastic gland. Her fetal well-being was constantly monitored and it was normal. Patient was discharged and FNAC of thyroid nodule was scheduled. But patient presented to the emergency department, before her scheduled visit, at the 27^{th} week of gestation with complaints of severe flank pain, decreased output in the nephrostomy tube, and pins and needles sensation on the face. Her serum calcium level was raised to 14.1 mg/dL. Multidisciplinary teams of obstetricians, ENT, endocrinology, and nephrology were taken on board. Due to the refractory nature of hypercalcemia, parathyroidectomy with on-table parathyroid hormone assays was recommended. Right thyroid lobectomy was done as it was asymmetrically enlarged with centrally hypodense and marginally calcified nodule, and the left inferior parathyroid gland was spared. After removal of the right superior, right inferior, and left superior parathyroid glands, her serum intact PTH assays dropped to 21 pg/mL. During the procedure, feto-maternal surveillance was done constantly and it was unremarkable. Post-operatively, maternal calcium levels were checked, and there was no subsequent requirement for calcium replacement. Histopathology of the right thyroid nodule was consistent with parathyroid adenoma, remaining parathyroid glands showed unremarkable parathyroid tissue with benign thyroid tissue seen in the right inferior parathyroid gland. Postoperatively, the patient remained stable and her serum calcium levels dropped to 9.3 mg/dL. On her subsequent OPD follow-ups, serum calcium levels remained within stable ranges and the patient remained asymptomatic. Later on, a healthy baby was delivered via spontaneous vaginal delivery at 38 weeks of gestation. The baby was monitored for neonatal hypocalcemia, however, his serum calcium levels remained within normal range.

3. Discussion

Primary hyperparathyroidism is characterized by hypercalcemia in the presence of raised or inappropriately normal PTH levels. However, physiological changes of pregnancy can mask its diagnosis, such as hypoalbuminemia with increased GFR, calcium transport across the placenta, and estrogen-mediated inhibition of PTH-mediated bone resorption [1]. All of these can lead to falsely low serum calcium values. Also, the diagnostic radiological modalities are limited in pregnancy, which is required to localize parathyroid tissue, due to the risk of radiation injury to the fetus [2].

Maternal complications of hypercalcemia include nephrolithiasis, recurrent urinary tract infections, hyperemesis, preeclampsia [6,7], and even pancreatitis [8]. These outcomes are relatively uncommon with mild hypercalcemia and treatment is usually based on the severity of hypercalcemia along with maternal age, complications, and duration of pregnancy. Similarly, neonatal complications include hypocalcemia, tetany secondary to fetal PTH suppression, preterm birth, low birth weight, and even stillbirth in case of severe hypercalcemia [6].

There is a 3 to 5-fold increased risk of miscarriage, which is more prevalent in patients with serum calcium greater than 11.42 mg/dL [1]. In pregnancy, total serum calcium tends to be slightly low due to plasma volume expansion, and the upper limit of normal total serum calcium in pregnancy is 9.5 mg/dL. However, normal pregnancy has not much impact on ionized serum calcium. Ideally, in women with PHPT, parathyroidectomy should be done prior to conception [9]. For individuals with asymptomatic PHPT, who do not meet the criterion for surgical intervention, parathyroidectomy can still be done, as it is the only definitive therapy [2]. Women of reproductive age, with an underlying disorder of PHPT, should be aware of the associated risks and complications. Pregnancy should be deferred until curative surgery is performed and serum calcium levels have returned to normal baseline. Because pre-operative localization of parathyroid adenomas during pregnancy remains challenging due to the limitation of imaging studies due to the risk of radiation injury to the fetus [2].

There are multiple reports of successful parathyroidectomy done during the second trimester; however, there is only limited data available on third-trimester parathyroidectomy. Parathyroidectomy during the third trimester has been associated with a greater risk of preterm delivery, neonatal hypocalcemia, and stillbirths [10]. However, later it has been suggested that these complications are associated with prolonged maternal hypercalcemia [11]. As seen from our case history that third-trimester parathyroidectomy, if performed using a sound surgical technique with greater intraoperative judgment, can surpass all feto-maternal risks.

When feasible, a minimally invasive approach rather than open procedures and intraoperative PTH monitoring is recommended [12], as done in our patient. A multidisciplinary approach will assist endocrinologists, obstetricians, surgeons, and anesthetists in this difficult decision-making process and optimizing treatment options for both mother and child [9].

4. Conclusion

As this disease has a marked impact on maternal and fetal morbidity and mortality, we, therefore, recommend considering parathyroidectomy regardless of the gestational age of the fetus, if all efforts at medical management prove unsuccessful or if there are fetal and maternal complications. Our case report supports this concept, but still, further data is required to refine guideline recommendations on parathyroidectomy during pregnancy.

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Statement of Competing Interest

It is stated that the authors have no competing interests

List of Abbreviations

PHPT: Primary hyperparathyroidism
PTH: Parathyroid hormone
FNAC: Fine needle aspiration cytology
GFR: Glomerular filtration rate

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