

Case Report

Primary hyperparathyroidism in pregnancy and review of literature

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Abstract

Primary hyperparathyroidism (PHPT) is rare condition during pregnancy; however, it can carry significant risks to both mother and foetus during and after the pregnancy. The definitive treatment is parathyroidectomy undertaken preferably in the second or early third trimester. A case of asymptomatic PHPT diagnosed and treated by parathyroidectomy in the third trimester is described.

Keywords: Hyperparathyroidism, Parathyroid adenoma, hypercalcaemia, pregnancy.

Introduction

PHPT is an uncommon condition, usually diagnosed in people in their fifth or sixth decade of life. Its prevalence in the general population is 0.15%. Although the exact incidence during pregnancy is not known, the incidence of PHPT in women of child bearing age is estimated to be 8 cases per 100,000 per year.¹ Physiological changes associated

with pregnancy make this condition difficult to diagnose, and 80% of affected pregnant women are found to be asymptomatic. The pregnant female is at a risk of significant pregnancy problems and complications ranging from an uncomplicated delivery to miscarriages, stillbirth or even neonatal death.^{1,2} It is therefore important for the obstetrician, surgeon, paediatrician and endocrinologist to be aware of this condition, and its potential complications to define a clear approach for its management.

We present a case of asymptomatic primary hyperparathyroidism treated by parathyroidectomy in the third trimester, in a mother after the development of tetany in a new born infant.

Case Report

A 23-year-old woman, gravida 2, Para 1, was booked at 19 weeks gestation. Her previous pregnancy was uneventful, but at 3 months of age her daughter had had seizures and was found to have low calcium and vitamin D

levels with normal Parathyroid hormone (PTH) levels. She was given calcium and vitamin D therapy. The mother was also evaluated and found to have calcium levels of 10.6mg/dl (normal range 8.6-10.5) borderline high and very low Vitamin D levels <1.1ng/ml (Normal range => 30ng/ml). PTH was not done. She was given intramuscular injection of 600,000 IU vitamin D once a month for six months. After treatment her vitamin D level was 23.6 ng/ml.

On the basis of the previous history of seizures in the infant, she was investigated in the index pregnancy when vitamin D level was normal (28.92 ng/ml) and calcium levels were raised (12.7 mg/dl). She was referred to the endocrinologist.

Further investigation revealed raised PTH 224 pg/mg (normal 18-67) with decreased serum phosphorus and magnesium (1.6 mg/dl) with normal urinary calcium (238 mg/24hour) and renal functions. An Ultrasound scan of the thyroid and parathyroid revealed normal texture of both lobes of thyroid and a hypoechoic mass lesion measuring 8.4 X 6.4 mm seen on the posterior-inferior to lower pole of left thyroid lobe. Colour Doppler showed normal flow. The diagnosis of primary hyperparathyroidism was made on the basis of biochemical and radiological investigations at 22 weeks of gestation.

Patient consented for Parathyroidectomy after 5 weeks due to fear of complications. A left inferior parathyroidectomy was performed at 27 weeks gestation with cyclogest given postoperatively as a tocolytic drug. Transient hypocalcaemia was observed in the postoperative period and calcium carbonate 2gm daily was started. Calcidol 0.25 mcg was also given orally to prevent hypocalcaemia. Histopathology confirmed a benign adenoma weighing 0.3 gm. The foetus was monitored by serial growth scans and remained normal. Patient opted for an elective caesarean section at 38 gestational weeks and delivered a healthy baby boy weighing 3 kilogram with good Apgar scores. Her postoperative period was uneventful. She is currently maintaining a calcium level of 9.0 dl/ml on one gram calcium intake per day. The baby was also monitored with calcium level and maintained his calcium level without development of any seizure yet at the age of ten months.

Discussion

Primary hyperparathyroidism in pregnancy needs to be recognized and treated due to the risks it confers to both mother and foetus. In the mother, the symptoms of hypercalcaemia secondary to hyperparathyroidism are similar to those in the non-pregnant patient.³ Maternal and foetal complication rates have been quoted to be as high as 67% and 80% respectively.^{4,5} Nephrolithiasis is the most common symptomatic presentation with an increased

incidence of 24-36% during pregnancy.⁶

Approximately 40% of patients with PHPT are hypercalciuric, and most of the remaining patients have normal values.⁷ The calcium excreted in a 24-h urine collection varies with age, sex, and race, and one 24-h collection does not capture the large variability in the measurement, therefore most studies on PHPT use serum calcium and PTH for assessment.⁸

Other complications include bone disease (osteitis fibrosa cystica), pancreatitis and hyperemesis gravidarum. Potentially, the most serious maternal complication is hypercalcaemic crisis, which classically presents with nausea, vomiting, weakness, dehydration and altered mental state changes. There can also be a rapid progression to uraemia, coma and death.^{2,4} Other manifestations of PHPT include spontaneous miscarriage, intrauterine growth retardation, low birth weight, premature delivery and intrauterine foetal death. In the postpartum period, maternal hypercalcaemia can worsen due to the removal of the foetal demand for calcium. Untreated hyperparathyroidism has 80% foetal complication rate.⁶ The incidence of a neonatal complication has been reported as high as 53% of which 27 - 31% is neonatal death.^{3,5}

Symptomatic PHPT is rarely detected in pregnancy due to the physiological changes that mask the symptoms, this includes maternal blood volume expansion, hypoalbuminaemia, increased foetal calcium requirements, and increased calcium clearance.

Calcium metabolism in pregnancy is a dynamic process. Maternal serum calcium falls by about 10% in pregnancy; however as the serum albumin falls by 20%, the ionized calcium remains unchanged. Foetal 1, 25-dihydroxyvitamin D, synthesized in foetal kidney and placenta, acts as the major stimulus and regulator of calcium transfer across the placenta.

It increases maternal gastrointestinal absorption of calcium by 150mg -400mg daily, additionally maternal urinary excretion is also increased from 90 to 300 mg daily. Major foetal calcium demands of approximately 25-30g, are required in the 3rd trimester for skeletal tissue mineralization. This requires an active transport of calcium across the placenta and the foetal serum calcium remains higher than maternal blood.

Primary hyperparathyroidism results in high concentrations of foetal serum calcium that acts to suppress the parathyroid glands. Foetal calcitonin concentrations are high to encourage bone mineralization. At birth however, the neonate is suddenly deprived of this source of calcium. It is incapable of mobilizing calcium from bone owing to the low concentrations of parathyroid hormone and high

concentrations of calcitonin. Acute neonatal hypocalcaemia results in tetany and convulsions, usually at 5 to 14 days of age. If the infant is breast fed, tetany can be delayed by one month or more.^{2,9}

Diagnosis of primary hyperparathyroidism should be confirmed by elevated serum calcium and PTH levels. Preoperative imaging by ultrasound of the parathyroid glands is recommended. Parathyroid ultrasound has a sensitivity of 69% and specificity of 94% and is safe in pregnancy. The gold standard is Technetium-99m sestamibi and ultrasound, with a combined sensitivity of 94.5%.¹⁰ However, Technetium-99m sestamibi is contraindicated in pregnancy and mostly an ultrasound will suffice.

Other causes of hypercalcaemia like excessive ingestion of calcium and vitamin D, thiazide diuretics, lithium therapy, sarcoidosis and haemoconcentration must be ruled out. Studies suggest that the foetal mortality rate can be reduced by a factor of four if operative cure is achieved.^{5,6}

Management:

Treatment of hyperparathyroidism during pregnancy should be individualized, based on the severity of disease, symptoms, and gestational age of the foetus. A significant decline in maternal and peri natal complications may be achieved with a high index of suspicion, appropriate diagnosis, and timely management of mothers. In certain situations intervention may be required, but excision of parathyroid adenoma remains the only definitive treatment.

In most reported cases, the adenoma accounts for 90% of primary hyperparathyroidism, carcinoma for 2% and hyperplasia (8-9%) for the remaining number of cases.³

Role of medical therapy in pregnancy:

Medical therapy in pregnancy for symptomatic primary hyperparathyroidism has been discouraged, due to safety issues of drug therapy, and the suboptimal control of serum calcium which leads to a high foetal loss rate.⁶

However in symptom-free patients or those with no radiologically identifiable parathyroid adenoma or those with mild hypercalcaemia diagnosed in 3rd trimester, may be managed medically, postponing operation until after delivery. If conservative management is considered intensive maternal and foetal surveillance should be initiated.

Medical therapy primarily involves stabilizing the patient with hydration, limiting calcium intake, correcting electrolyte imbalance, administration of magnesium sulfate, oral phosphate and calciuretic diuretics.^{2,3}

Role of surgery:

Symptomatic and poorly controlled hypercalcaemic patients should be offered surgical resection which can be carried out in the second or early third trimester.

Earlier reports have suggested low complication rates, most common being laryngeal nerve injury or hypoparathyroidism, with a quoted mortality rate of 0.1%.⁶ However a recent review of surgically managed patients who underwent parathyroidectomy even in the third trimester, found it to be effective and safe with reduced maternal and foetal risk for complications. Post operative hypocalcaemia can be easily managed with calcium and vitamin D supplementation.^{6,11}

Conclusion

Primary hyperparathyroidism during pregnancy though rare, is associated with high maternal, foetal and neonatal mortality. Increased awareness, earlier detection, and better management are the key to decreasing its complications. A surgical option should be considered in view of a poor control of the hypercalcaemic state in pregnancy by medical or conservative management. Hyperparathyroidism during pregnancy may be safely treated with parathyroidectomy when performed during the second trimester or early third trimester.

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