Parathyroid carcinoma masquerading as morning sickness in pregnancy

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ABSTRACT

Incidence of primary hyperparathyroidism (PHP) in pregnancy is 8/100,000 population/year with less than 200 cases reported. Physiological changes associated with pregnancy make a diagnosis of PHP difficult and 80% are asymptomatic. High index of suspicion is required as physiological hypocalcemia related to hemodilution, increased glomerular filtration rate resulting in maternal hypercalciuria and gestational hypoalbuminemia can mask hypercalcemia of PHP. Maternal and fetal complication rates are high. Early recognition followed by appropriate management and treatment significantly reduces complications. Here, we present a rare case of parathyroid carcinoma in pregnancy and highlight the difficulties in diagnosis given the non-specific symptoms related to hypercalcemia. We have also discussed the management of PHP during the pregnancy. PHP is a preventable cause of fetal and maternal morbidity and mortality.

Key words: Hypercalcemia, hyperparathyroidism in pregnancy, morning sickness, parathyroid carcinoma

INTRODUCTION

Primary hyperparathyroidism (PHP) is a rare life-threatening condition that can present during the pregnancy.[1] Most of the cases are due to parathyroid adenoma, but rarely parathyroid carcinoma may be the cause of PHP.[2] Diagnosis can be difficult to establish during the pregnancy, given the non-specific symptoms related to hypercalcemia. Here, we present a case of parathyroid carcinoma diagnosed during the pregnancy.

CASE REPORT

A 10-week-pregnant female patient had presented with nausea and vomiting in antenatal clinic. She had experienced an unremarkable pregnancy so far. She was diagnosed as having morning sickness and prescribed multivitamins and symptomatic treatment to which she did not respond. She was referred to Gastroenterologist when she started having abdominal pain. Evaluation for abdominal pain revealed hypercalcemia. There was no history of calcium disorders, kidney stones, fractures, osteoporosis or any drug ingestion, which could lead to hypercalcemia.

On examination, there was no goiter or palpable nodule in the neck. She had no bone tenderness. Initial laboratory evaluation revealed severe hypercalcemia with a corrected calcium level 14.9 mg/dl (reference range 8.5-10.3 mg/dl) and a phosphorous level of 1.9 mg/dl (2.4-4.1) with a normal renal function. Her 25-hydroxy vitamin D levels were 27.6 ng/ml. Her parathyroid hormone (PTH) level was 768 pg/ml (10-60 pg/ml) and a urinary calcium level of 879 mg/24 h (reference range: 100-300 mg/24 h). Laboratory work-up was inconsistent with vitamin D intoxication, milk alkali syndrome, sarcoidosis, hyperthyroidism or malignancy.

Ultrasound of the neck was carried out, which showed a 4.05 cm × 3.39 cm × 2.5 cm sized left inferior parathyroid adenoma as shown in Figure 1. Morphology of thyroid gland was normal. Magnetic resonance imaging of neck...
confirmed a mass of the same size arising from the parathyroid gland as shown in Figures 2 and 3. Rest of the neck tissue and upper thorax was unremarkable. Sestamibi scan could not be performed because of pregnancy.

An elective minimally invasive parathyroidectomy of the enlarged parathyroid gland was planned at 14 weeks of pregnancy. During the surgery, an enlarged parathyroid gland was located behind the left lobe of thyroid gland and was well-encapsulated and easily separated from thyroid. There was a remarkable drop in the PTH levels from 768 pg/ml to 25 pg/ml at 10 min after the removal of the enlarged parathyroid gland as measured intraoperatively. Post-operatively, calcium and PTH level was 9.4 mg/dl and 38.5 pg/ml respectively. Transient drop in the serum calcium during the post-operative period was managed with oral and intravenous calcium supplementation. The patient's calcium stabilized after 4 days and was discharged and counseled for regular and frequent endocrine and antenatal follow-up. Pathological evaluation of the resected mass demonstrated parathyroid carcinoma with vascular and capsular invasion as shown in the Figures 4 and 5. However, on follow-up there is no recurrence of hypercalcemia and repeat ultrasound is not suggestive of any lymph node enlargement or any other evidence of malignancy.

**DISCUSSION**

Diagnosis of PHP in pregnancy becomes difficult due to two reasons; firstly, 80% are asymptomatic and secondly the clinical features of hypercalcemia can be easily confused with non-specific symptoms in pregnancy unless more specific symptoms like pathological fracture or renal stones manifest, which themselves are rare nowadays. Biochemically, pregnancy makes the diagnosis of hypercalcemia challenging due to factors such as physiological hemodilution, hypoalbuminemia and maternal hypercalciuria due to an increase in glomerular filtration rate.

Diagnosis of PHP in pregnancy applies the same criteria as in non-pregnant adults namely, an elevated total corrected calcium level (>9.5 mg/dl) or ionized calcium level, hypophosphatemia (<2.5 mg/dl) and an elevated serum PTH level in the absence of other causes of hypercalcemia. It is necessary to exclude familial hypocalciuric hypercalcemia and other hereditary endocrinopathies. Ultrasonography of the neck is the investigation of choice during pregnancy for localization of parathyroid adenomas with a sensitivity of 69% and specificity 94%.[2]

PHP also poses a grave danger to fetus if untreated hence necessitating an immediate and complete expert management by a multidisciplinary approach. PHP leads to maternal complications in 2/3 of cases with nephrolithiasis, bone disease and pancreatitis being most common.[3] Other less frequent maternal complications include hyperemesis gravidarum, preeclampsia, tremors, constipation, depression, blurred vision, uremia, seizures and coma.[3] However, the gravest of all complications are
hypercalcemic crises in antenatal and hypocalcemic tetany and seizures in immediate postnatal period.[2]

Due to the paucity of specific guidelines, management of hyperparathyroidism during pregnancy needs to be individualized considering clinic-biochemical issues and fetal well-being. A minimally invasive parathyroidectomy in the second trimester is the gold standard in managing PHP during pregnancy.[3]

Parathyroid carcinoma is one of the rarest of endocrine cancers with higher prevalence in patients with the chronic kidney disease and neck irradiation.[4] They are slow growing tumors presenting with hypercalcemia and having a tendency to recur locally in 40-60% of cases. They occur with equal propensity in males and females and at a younger age, are larger in size and associated with profound renal, metabolic, neuromuscular, rheumatologic, gastrointestinal and cardiovascular manifestations.[4] Microscopically, the cells resemble watermelon seeds and show vascular and capsular invasion in most of the cases, but these features are not absolutely conclusive.[4]

**CONCLUSION**

PHP is a preventable cause of fetal and maternal morbidity.

A high index of suspicion is required as multiple factors can mask hypercalcemia. Maternal hypercalcemia induces profound fetal parathyroid gland suppression leading to a fatal neonatal tetany. Our case highlights the significance of timely recognition and effective management of PHP in pregnancy, leading to optimization of both maternal and fetal outcomes.

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