CASE REPORT

Primary Hyperparathyroidism with Severe Hypercalcemia in Pregnancy Complicated by Acute Pancreatitis; A Rare Case Report And Literature Review

Nadiah M. Alhabardi

***Correspondence**:* MD, Specialist in Ob Gyn, Prince Sultan Military Medical City, Riyadh
E-mail:n-hab@hotmail.com, Mobile: 00966553999984

Abstract:

Background: Primary hyperparathyroidism with pancreatitis is very rare during pregnancy. The pregnant state presents a challenge to the diagnosis of hypercalcemia related to the many physiological changes that occur.

Objective: To report a case of primary hyperparathyroidism in a pregnant patient, and to advocate a successful management with satisfactory outcome.

Results: A 36-year-old multigravida Saudi woman presented during her 34th week of gestation with a five days history of epigastric pain, nausea and vomiting.Diagnosis was made as Primary hyperparathyroidism with severe hypercalcemia in pregnancy complicated by acute pancreatitis.

She was initially managed with conservative medical measures and due to the failure of medical management, a multidisplinary team decided to terminate the pregnancy by cesarean section and to do parathyroidectomy at the same time at 34-weeks gestation. The maternal and fetal outcome was quite satisfactory. To the best of our knowledge, this is one of the rare case report in the literature with such finding and satisfactory outcome.

Conclusions: Early diagnosis and appropriate management of Primary Hyperparathyrodisim (PHP) during pregnancy is important for better outcome. Multidisciplinary management decisions can significantly reduce the morbidity and mortality associated with the disease during pregnancy.

Keywords: hyperparathyroidism, pancreatitis, pregnancy, hypercalcemia.

Introduction:

Primary hyperparathyroidism (PHP) is the third most common endocrine disorder after diabetes and thyroid disease, and women are affected twice as often as men [1,2]. Most patients suffering from PHP are older than 45 years, but 25% are diagnosed in their childbearing years.

PHP has been reported to lead to maternal complications in 2/3 of cases [3]. The presentation of hypercalcemia in pregnancy related to PHP is variable and ranges from asymptomatic in 23% to symptoms such as nausea, vomiting, and anorexia in 36%, weakness and fatigue in 34%, and neurological/psychiatric manifestations in 26% based on a review of 70 women with PHP during pregnancy [4]. Other reports suggest that up to 80% of patient with hyperparathyroidism may be asymptomatic [5,4].

Acute pancreatitis is reported to be a serious but rare presentation of PHP in pregnancy. [6,7,8,] However, recent population-based studies have refuted this association. [9]

The preference for surgery over medical management (with oral phosphates, calcitonin, calcium wasting diuretics, etc) has been well established. [10]

Because of the significant maternal, fetal and neonatal risks outlined, and the improved safety of general anaesthetic during pregnancy, surgical management is increasingly recommended. [11] It is thought that the risks are outweighed by the benefits to reduce maternal serum calcium back to normal range. It is supported by research indicating that neonatal complication rates are 37% after medical treatment and only 10% after surgical intervention. [12]

Case Report:

A 36-year-old multigravida (G8P4A3) with a live and well children Saudi woman presented during her 34th week of gestation with a five days history of epigastric pain, nausea and vomiting.The abdominal pain was epigastric, dull in nature radiated to the back, exacerbated by eating and progressively increases over last 5 days.

The vomiting was severe and not projectile whatever she took orally, but not reported neither heamatemesis, change in bowel habit, history of fever and jaundice nor change in stool or urine color.

Her pregnancy was unremarkable up til this time. She denied any history of bone pain or fracture, renalstone, hematuria, joint pain, muscle pain or weight change, dysuria, constipation, polydipsia, polyuria, weight loss, anorexia, or muscle weakness during her pregnancy. She had no history of calcium disorders, kidney stones, fractures, osteoporosis or endocrinopathies. Also no history of cold intolerance or hotness, palpitation or shortness of breath, postural dizziness, headache or visual problems, skin eruption or hyperpigmentation. There were no reported history of lower abdominal pain, per vaginal bleeding and fetal movement was good.

Family history was negative for calcium disorders, kidney stones, fractures, osteoporosis, endocrinopathies or parathyroid disorders, but her father had esophageal cancer and her grandmother had a history of thyroid cancer.

She was taking folic acid and multivitamins. She was not taking thiazide diuretics, antacids, or lithium which could influence her calcium status. She was a housewife and all her children all are well.

The patient was unbooked in our hospital, and was followed in a private hospital and for the first time presented to our hospital in this pregnancy with this complain. Regarding her past medical history there was no history of diabetes mellitus, hypertension or any other chronic or endocrine disease.

On physical examination, she was conscious, oriented, in pain and distress and looked moderately sick. Her blood pressure was 114/56 mmHg, heart rate 85-110/min and regular, respiratory rate 18/minute, and temp 36.7ºC and oxygen saturation 98 %.

There were no palpable neck masses, jaw abnormalities, cervical or supraclavicular lymphadenopathy.

On abdominal examination, there was mild epigastric tenderness and the uterus was 34weeks consistent with her gestational age. She had no kyphosis or bone tenderness. There was significant proximal myopathy with no bony tenderness. The remainder of the systemic examination was unremarkable.

The following differential diagnoses were considered acute gastroenteritis, peptic ulcer disease, acute cholecystitis, acute pancreatitis, gestational diabetes with diabetic keto acidosis, inferior myocardial infarction and abruptio placentae.

Initial laboratory evaluation revealed severe hypercalcemia with a calcium level

16.3 mg/dL (reference range 8.5–10.3), albumin 37g/L (3.2–5.5), and a phosphorous level 0.61mg/dL (2.4–4.1). She had normal renal function, her 25 hydroxy vitamin D was 19.1 nmol/L (8.9–46.7).

On further workup, she was found to have an elevated PTH level of 697pg/mL (16–48pg/mL) and serum amylase was 932 U/L (normal range: 28-100 U/L).Complete blood count and liver function tests were normal. She was biochemically euthyroid. Lipid profile was within normal ranges.

U/S abdomen showed diffusely hypoechoic pancrease suggestive of pancreatitis, bilateral renal medullary nephrocalcinosis and there were no gall stones and normal common bile duct (CBD).

Ultrasonography of her neck revealed a two well defined hypoechoic nodules noted on the posterior aspect of left lobe highly suggestive of parathyroid adenoma (Figure 1).

An obstetrical ultrasound confirmed alife single intrauterine gestation consistent with 34 week of gestation.

Based upon her previously mentioned history and investigations a diagnosis of Primary hyperparathyroidism with severe hypercalcemia in pregnancy complicated by acute pancreatitis was made.

She was initially managed with conservative measures namely: eucalcemic diet and aggressive hydration with minimal improvement in her clinical or biochemical status. Due to her persistent symptomatic hypercalcemia despite conservative measures a multidisciplinary team was involved including an endocrine surgeon, an obstetrician, an endocrinologist, a neonatologist and an anestheologist for their opinion for further management. They decided to terminate the pregnancy by cesarean section and to do parathyroidectomy at the same time at 34-week gestation. Outcome was Baby girl, fetal weight 2090 g, Apgar score 7 and 8, admitted to neonatal intensive care unit (NICU) with respiratory distress syndrome and had CPAP for 5 days and neonatal jaundice for which she had phototherapy for 1 day and hypercalcemia 1 reading and hypomagnesemia 1 reading.

There was a marked drop in the intraoperative PTH levels after the removal of the enlarged parathyroid gland, confirming a successful operation. Pathological evaluation of the resected mass demonstrated an enlarged parathyroid gland. Histopathologic examination of the parathyroid gland was consistent with a

parathyroid adenoma (Figure 2). The patient was discharged home at 4 postoperative daysin good condition with a normal calcium level (2,58 mmol/l) and a life baby.

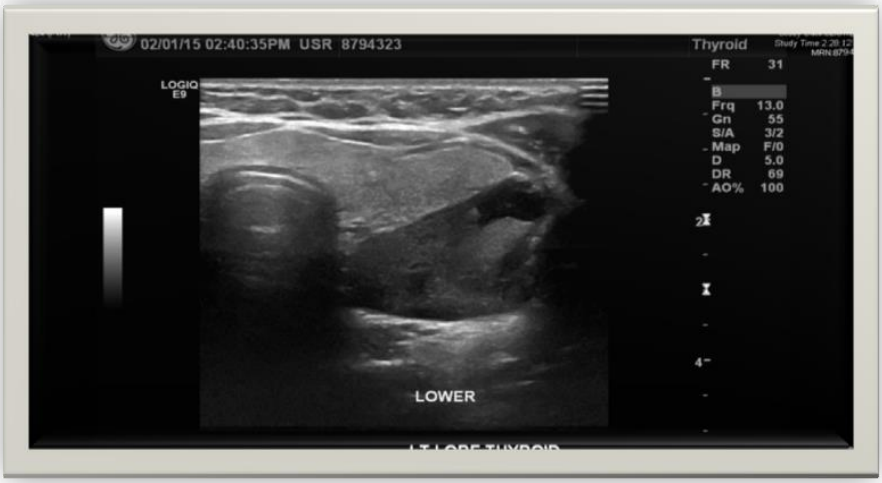

Figure 1: Ultrasonography of her neck revealed a two well defined hypoechoic nodules noted on posterior aspect of left lobe highly suggestive of parathyroid adenoma.

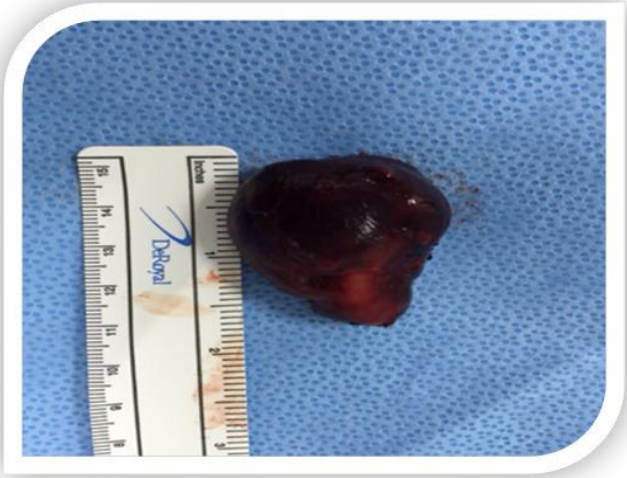

Figure 2: Enlarged parathyroid glandconsistent with a parathyroid adenoma

Discusion:

This case highlights the significance of timely recognition and effective management of PHP in pregnancy, leading to optimization of both maternal and fetal outcomes.

Maternal complication rates related to PHP during pregnancy have been reported to be as high as 67% [3], and fetal complications are reported to occur in up to 80% cases [13]. Early identification and management of this condition in pregnancy can significantly reduce fetal, neonatal, and maternal morbidity and mortality associated with this important condition.

A diagnosis of such cases is difficult in pregnancy because the clinical picture confuses with pregnancy physiology. The work up done for this case has been appreciated; depending on clinical presentation and laboratory findings. A diagnosis of PHP in pregnancy should be considered with the simultaneous findings of 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 [14]. Additionally, the diagnosis should be considered in any patient who presents with the classic features of hyperparathyroidism such as pancreatitis, fractures, or peptic ulcer disease (PUD) [15].

Ultrasonography for the neck and abdomen done for this case has played a major role to reach the diagnosis. Ultrasonography of the neck is the investigation of choice during pregnancy for localization of parathyroid adenomas with a sensitivity of 69% and a specificity of 94% [16].

As the diagnosis was made in the 3rd trimester, a discussion with the patient was undertaken regarding the risks and benefits of surgery. Some authors advocating that surgery in the 3rd trimester is safe and reduces fetal complications from maternal PHP [17]. In our setting we have enhanced preoperative localization, improved surgical procedures, and the ability to perform rapid intraoperative serial PTH levels. In such situations the operative time can be dramatically reduced [18,19]. There is only one other prior case report published of the use of intraoperative PTH monitoring to confirm the successful surgical removal of an adenoma in a pregnant patient [20].

Surgery was performed, although it is reported that surgery during the 3rd trimester it is associated with a higher risk of neonatal complications and

mortality [21]; however, it is acceptable when the benefit outweighs the risk [17,22]. In this case because all efforts failed and urgent parathyroidectomy and cesarean section were done. The management plan adopted was satisfactory with appreciated maternal and fetal outcome.

References:

1. Wermers RA, Khosla S, Atkinson EJ, Achenbach SJ, Oberg AL, Grant CS, Melton LJ., 3rd Incidence of primary hyperparathyroidism in Rochester, Minnesota, 1993–2001: an update on the changing epidemiology of the disease. J Bone Miner Res. 2006;21(1):171–177.
2. Kokrdova Z. Pregnancy and primary hyperparathyroidism. J Obstet Gynaecol. 2010;30(1):57–59.
3. K. C. Kort, H. J. Schiller, and P. J. Numann, "Hyperparathyroidism and pregnancy," American Journal of Surgery, vol. 177, no. 1, pp. 66–68, 1999.
4. M. J. Carella and V. V. Gossain, "Hyperparathyroidism and pregnancy: case report and review," Journal of General Internal Medicine, vol. 7, no. 4, pp. 448–453, 1992.
5. H. Heath, S. F. Hodgson, and M. A. Kennedy, "Primary hyperparathyroidism. Incidence, morbidity, and potential economic impact in a community," The New England Journal of Medicine, vol. 302, no. 4, pp. 189–193, 1980.
6. Chamarthi B, Greene MF, Dluhy RG. A problem in gestation. N Engl J Med 2011;365:843–8
7. Krysiak R, Wilk M, Okopien B. Recurrent pancreatitis induced by hyperparathyroidism in pregnancy. Arch Gynaecol Obstet 2011;284:531–4
8. Hong MK, Hsieh CTC, Chen BH, et al. Primary hyperparathyroidism and acute pancreatitis during the third trimester of pregnancy. J Mater Fetal Med 2001;10:214–18
9. Khoo TK, Vege SS, Abu-lebdeh HS, et al. Acute pancreatitis in primary hyperparathyroidism: a population-based study. J Clin Endocrinol Metab 2009;94:2115–18
10. Truong MT, Lalakea ML, Robbins P, et al. Primary hyperparathyroidism in pregnancy: a case series and review. Laryngoscope 2008;118:1966–9
11. Schnatz PF, Curry SL. Primary hyperparathyroidism in pregnancy: evidence based management. Obstet Gynaecol Surv 2002;57:365–76
12. Kelly TR. Primary hyperparathyroidism during pregnancy. Surgery 1991; 110:1028–33
13. F. L. Delmonico, R. M. Neer, and A. B. Cosimi, "Hyperparathyroidism during pregnancy," American Journal of Surgery, vol. 131, no. 3, pp. 328–337, 1976.
14. J. M. Lopez and C. B. Fardella, "Primary hyperparathyroidism: changes on biochemical and hormonal profile related to pregnancy," Journal of Endocrinological Investigation, vol. 12, no. 2, pp. 127–129, 1989.

15. A. Kristoffersson, S. Dahlgren, F. Lithner, and J. Jarhult, "Primary hyperparathyroidism in pregnancy," Surgery, vol. 97, no. 3, pp. 326–330, 1985.
16. C. C. Reading, J. W. Charboneau, and E. M. James, "High-resolution parathyroid sonography," American Journal of Roentgenology, vol. 139, no. 3, pp. 539–546, 1982.
17. F. Schnatz and S. Thaxton, "Parathyroidectomy in the third trimester of pregnancy," Obstetrical and Gynecological Survey, vol. 60, no. 10, pp. 672–682, 2005
18. P. F. Schnatz and S. L. Curry, "Primary hyperparathyroidism in pregnancy: evidence-based management," Obstetrical and Gynecological Survey, vol. 57, no. 6, pp. 365–376, 2002.
19. R. A. Sofferman, J. Standage, and M. E. Tang, "Minimal-access parathyroid surgery using intraoperative parathyroid hormone assay," Laryngoscope, vol. 108, no. 10, pp. 1497–1503, 1998.
20. P. Pothiwala and S. N. Levine, "Parathyroid surgery in pregnancy: review of the literature and localization by aspiration for parathyroid hormone levels.," Journal of Perinatology, vol. 29, no. 12, pp. 779–784, 2009.
21. M. J. Carella and V. V. Gossain, "Hyperparathyroidism and pregnancy: case report and review," Journal of General Internal Medicine, vol. 7, no. 4, pp. 448–453, 1992.
22. P. Pothiwala and S. N. Levine, "Parathyroid surgery in pregnancy: review of the literature and localization by aspiration for parathyroid hormone levels.," Journal of Perinatology, vol. 29, no. 12, pp. 779–784, 2009.