

Primary hyperparathyroidism in pregnancy - case report and review

Yves Muscat Baron, Rodianne Camilleri Agius,
Johann Craus, Alex Attard, Mario Cachia

Abstract

A twenty-six year old secundagravida booked her pregnancy at 14 weeks gestation. It was noted in the past obstetric history that the woman had lost her first child at 41 weeks gestation, delivering a stillborn baby weighing 4.2kg. At 34 weeks into the second pregnancy mild polyhydramnios was noted and the patient was admitted. During her hospitalisation the patient complained of having passed a small renal stone. Two serum calcium levels were found to be significantly elevated 3.36mmol/l and 3.2mmol/l. Serum parathormone was found to be significantly elevated - 247pg/ml (Normal levels: 12.0 - 72.0pg/ml) and an ultrasound scan of the neck confirmed the presence of a parathyroid adenoma. A parathyroidectomy was performed and the postoperative period was uneventful. The rest of the pregnancy was uneventful and at 38 weeks gestation a healthy child was delivered vaginally. In view of this woman's past history and the events occurring during the second pregnancy it may be useful to consider obtaining serum levels of calcium in cases of idiopathic stillbirth.

Keywords

Hyperparathyroidism, pregnancy, calcium,

Yves Muscat Baron*

Department of Obstetrics and Gynaecology,
Mater Dei Hospital
Email: yambaron@synapse.net.mt

* corresponding author

Case report

Mrs E. I. was a 26 year old foreign Caucasian woman who booked her second pregnancy at 14 weeks gestation. She gave an obstetric history indicating that she had sustained a stillborn child weighing 4.2 kg at 41 weeks gestation. In view of the adverse obstetric history, antenatal care was carried out at Mater Dei Hospital. The patient's body mass index during her booking visit in the first trimester was 23.3kg/m². Due to the past history of stillbirth and its elevated birthweight, an oral glucose tolerance was carried out at 28 weeks gestation and was found to be normal (American Diabetic Association) – fasting: 4.49mmol/l, 1st hour: 4.78mmol/l, 2nd hour: 3.95mmol/l and 3rd hour: 4.15mmol/l. In the previous pregnancy there was no history of a metabolic problem in particular impaired carbohydrate metabolism.

The pregnancy progressed uneventfully until 34 weeks gestation when mild polyhydramnios was noted clinically and this was confirmed ultrasonically (Amniotic Fluid Index: 23.5 cm - 90th centile). In view of this finding and the past obstetric history the patient was hospitalised for closer maternal-fetal surveillance. Growth ultrasound scans and Doppler flow studies were within normal limits. Blood glucose levels remained within the normal range. On the third day of hospitalisation the patient complained of having passed a small renal stone. There was no history of nephrolithiasis from either the patient's past history or family history.

Following the passage of the urinary calculus, two serum calcium levels were taken and found to be significantly elevated at 3.36mmol/l and 3.2mmol/l (normal range: 2.15 - 2.55mmol/l). In view of the hypercalcaemia, serum parathormone level was investigated and was also found to be significantly elevated : 247pg/ml (normal range: 12.0 - 72.0pg/ml). An ultrasound of the anterior aspect of the neck was performed and confirmed the presence of a 2.4cm x 1.1 cm left inferior lateral parathyroid adenoma. The thyroid gland was normal and no cervical lymphadenopathy was noted.

While the patient was still hospitalised an episode of elevated blood pressure (140/90mmHg) and two ++ proteinuria were noted on urinalysis. Renal function tests were within normal levels: urea 3.3mmol/l, creatinine 49µmol/l and the uric acid 342µmol/l. Ultrasonic investigation of both kidneys showed hydronephrosis of the right kidney while the left kidney was normal. No renal calculi were detected ultrasonically.

Steroids in the form of 12mg dexamethasone were administered to reduce the risk of foetal respiratory distress syndrome if premature delivery was necessitated. The steroid administration may have been also useful in attenuating the adverse effects hypercalcaemia may have on the pregnancy. The patient remained normotensive and the proteinuria resolved without resorting to anti-hypertensive treatment.

A dual consultation was sought from the departments of surgery and endocrinology, and it was recommended that the patient undergo neck exploration. A parathyroidectomy was performed removing a 2.5cm left parathyroid gland which was histologically confirmed to be a parathyroid adenoma. The postoperative period was uneventful with close monitoring of serum calcium levels. Postoperatively normal serum calcium levels (serum calcium 2.24mmol/l) ensued throughout the pregnancy. The rest of the pregnancy was uneventful until 38⁺4 weeks gestation when an unprovoked fetal heart deceleration was noted on cardiotocography. A decision was taken to induce the pregnancy and a healthy 3.08kg female child being delivered vaginally. Normocalcaemia for both mother and baby were confirmed in the postpartum period. The patient is being followed up by the Department of Endocrinology.

Discussion

In the general population the prevalence of primary hyperparathyroidism is 1.5 per 1000.¹ This condition is more commonly found in women and 25% of cases are diagnosed in women during the childbearing years.¹ The first case of parathyroid adenoma in pregnancy was recorded by Hunter in 1930 and the literature is relatively scanty with only about 109 cases reported in the medical literature.²

The condition can lead to increased risk of maternal and perinatal mortality if left undiagnosed.² The incidence of clinically significant complications resulting from delayed diagnosis or postponed surgery ranges from 17.6% to 23.5% in fetuses, including foetal or neonatal death, and 18.8% to 25.0% in mothers.³

Maternal complications may start early in pregnancy with intractable hyperemesis gravidarum⁴ and miscarriage.⁵ Maternal arrhythmias revealed clinically by palpitations and dyspnoea may result from hypercalcaemia-induced ventricular premature contraction bigeminy and trigeminy.⁶ Antepartum haemorrhage⁷ and preterm labour⁸ may also occur in pregnancies complicated by primary hyperparathyroidism. In the postpartum period the loss of the protective effect provided by the placental calcium transport mechanism may lead to significant maternal risk for the development of acute hypercalcaemia and possible crisis immediately after delivery.⁹

Pre-eclampsia including the HELLP syndrome has been shown to commonly complicate primary hyperparathyroidism in pregnancy.¹⁰ Hultin *et al* have shown that parathyroid adenoma prior to delivery is significantly ($p < 0.001$) associated with pre-eclampsia, resulting an adjusted odds ratio of 6.89 (95% confidence interval, 2.30 - 20.58).¹¹ Our case had a blood

pressure reading of 140/90mmHg and two pluses of proteinuria. After dexamethasone and following the parathyroidectomy the patient remained normotensive. It must be mentioned that this episode of high blood pressure may have been spurious reflecting the patient's understandably anxious state of mind. The proteinuria may have resulted from the nephrolithiasis and hydronephrosis.

The reason for the patient's hospitalisation was due to the clinical detection of mild polyhydramnios which was confirmed ultrasonically. Similar to adults, hypercalcaemia may induce polyuria also in the fetus and this may explain the polyhydramnios.¹² Progressive polyhydramnios itself may go on to cause preterm labour. The polyhydramnios did not worsen post-operatively, during the remaining four weeks of pregnancy. The presence of polyhydramnios and the passage of a urinary calculus raised the possibility of hyperparathyroidism. Such an event in pregnancy is exceptional but should be thoroughly investigated with serum calcium levels.¹³

During pregnancy the calcium requirements of the fetus amount to approximately 30 g of calcium to mineralise its skeleton and maintain normal physiological processes.¹⁴ About 80% of the calcium sequestered in the fetal skeleton at the end of gestation crosses the placenta during the third trimester and is mostly derived from intestinal dietary absorption of calcium during pregnancy.¹⁴ Pregnancy-related falls in total serum calcium are due to the reduction in the serum albumin, and, thereby, the albumin-bound fraction of the total calcium and the physiological haemodilution induced by pregnancy.¹⁵ The increased calcium requirements during pregnancy are attained by the doubling of intestinal calcium absorption.¹⁴

Recurrent miscarriage is known to occur in women with primary hyperparathyroidism and is associated with a 3.5-fold increase in miscarriage rates. Pregnancy loss often occurs in the late first trimester and second trimester.¹⁶ Pregnancy loss is more common as calcium levels exceed 2.85mmol/l, but can be seen at all elevated calcium levels.¹⁶ Intra-uterine growth retardation may occur in pregnancies with primary hyperparathyroidism. This may occur even after surgical treatment whereby severe placental calcification ensued and a severely intra-uterine growth restricted baby was born.¹⁷

Untreated cases of primary hyperparathyroidism during the neonatal period have included neonatal death, neonatal tetany and hyper/hypocalcaemia.¹⁸ Neonatal hypocalcaemia probably results from transient hypoparathyroidism consequent to abnormal suppression by fetal hypercalcaemia.

Medical treatment in pregnancy may be instituted in cases where surgery may be considered hazardous¹⁹ but the mainstay of treatment is surgical excision of the parathyroid adenoma.^{3,7,16,18} The first surgically treated case was reported in 1975 by Dorey and Gell, emphasising the diminished risk to both mother and fetus following parathyroidectomy.²⁰ Histological examination of a series by Schnatz *et al*³ revealed that parathyroid adenomas were detected in 81.2% of cases, hyperplasia in 6.3%, and carcinoma in 12.5%. The postoperative

incidence of clinically significant complications from surgery was as low as 5.9% in fetuses and 0% in mothers. Postoperative hypocalcemia was detected in 62.5% of mothers and 17.6% of their newborns. All cases were easily managed with calcium replacement.³ In our case, postoperative serum calcium levels remained within normal limits in both mother and neonate.

This paper confirms that parathyroidectomy performed in the third trimester of pregnancy is effective. Postponing surgery may risk an adverse maternal and fetal outcome. Moreover considering this woman's obstetric history and the literature review, estimation of serum calcium may prove useful in cases of idiopathic stillbirth and recurrent miscarriage.

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