Case Reports

Neonatal Outcome in Maternal Hyperparathyroidism

K.P. Sanghvi
J. Pinto
R.H. Merchant

Primary hyperparathyroidism is unusual during pregnancy (l). The incidence of primary hyperparathyroidism during pregnancy is unknown, but in women of childbearing age it is approximately eight cases per 100,000 women per year (2). Between 1930 and 1993, approximately 114 cases of pregnancy with hyperparathyroidism were reported in the world literature (3-12). The influence of hyperparathyroidism on pregnancy can vary from an uncomplicated gestation, delivery, and neonatal period, to abortion, stillbirth or maternal and neonatal morbidity and mortality (3,4,13). The symptoms of primary hyperparathyroidism are varied and nonspecific and may mimic symptoms of normal pregnancy leading to many cases being undiagnosed (2,6). The present report discusses the course and outcome of three cases of maternal hyperparathyroidism during pregnancy.

Reprint requests: Dr. R.H. Merchant, Director, Neonatal Services, Nowrosjee Wadia Maternity Hospital Parel, Bombay 400 012.

Received for publication: February 7,1996; Accepted: May 31,1996

Case Reports

Case 1: A 26-year-old woman, gravida 3, para 1, presented at 26 weeks gestation with generalized joint pains, nausea, vomiting, anorexia, and pain in the calves. She was found to be normal on examination. Her ailment was attributed to normal pregnancy and her oral iron preparation was changed. Her symptoms continued unabated and at 28 weeks of gestation she developed a urinary tract infection which was treated. On her monthly antenatal visit at 30 weeks of gestation, she was found to have a weight loss of 1 kg and appeared weak. An ultrasound for fetal well-being showed no evidence of fetal growth retardation, but an incidental observation of the maternal kidneys showed bilateral diffuse nephrocalcinosis and renal stones. Biochemical investigations which followed are shown in *Table I.* An ultrasound scan of her neck revealed an enlarged left inferior parathyroid gland suggestive of adenoma. Repeat serum calcium levels done weekly ranged from 11 mg/dl to 12.5 mg/dl. A parthyroidectomy was done under a cervical block at 35 weeks of gestation. A left inferior parathyroid gland weighing 8 g and 3 cm x 2.5 cm x 1.5 cm in size was removed. Histopathological examination confirmed the diagnosis of a parathyroid adenoma. She complained of generalized mild tingling sensation around 12 hours post-operative, when her serum calcium was 8.1 mg/dl. This was treated by giving intravenous calcium gluconate. The serum calcium levels remained within normal range thereafter. She went on to deliver a full term female

child weighing 3200 g by an elective Cesarean section at 39 weeks of gestation. The infant's serum calcium levels remained within normal range and are shown in *Table II.* This child is developmentally normal at 4 years of follow up.

Case 2: A 30 year old primigravida noticed a painful swelling of the left knee joint at 24 weeks gestation. An X-ray of the left lower limb revealed osteolytic areas in the upper l/3rd of the left tibia suggestive of multiple myelomatosis, fibrous dysplasia or metastasis. A CT scan of the lesion demonstrated multiple osteolytic lesions in the left tibia associated with endosteal erosion suggestive of fibrous dysplasia. An excision biopsy was done at 28 weeks of gestation. Histopathological examination showed a combination of fibrous dysplasia and fibrous histiocytoma with a large population of osteoclasts, suggestive of osteitis fibrosa cystica. Investigations revealed hypercalcemia *(Table I).* An obstetric ultrasonography at 30 weeks of gestation showed a normally growing fetus. Ultrasound scan of neck showed an enlarged right inferior parathyroid gland 15 mm x 13 mm x 5 mm in size. A right inferior parathyroidectomy was done at 34 weeks gestation. Twelve hours post-operative, the patient developed symptomatic hypocalcemia with tetany and was treated with intravenous 10% calcium gluconate. Her serum calcium levels 12 hours post-operative was 6.8 mg/dl. She was advised calcium supplements for the rest of her pregnancy. She went into spontaneous labor at 38 weeks gestation and delivered a healthy female child of a birth weight of 2.8 kg. This child is normal at 2 years of follow up. Maternal and infant calcium levels are indicated in *Table II.*

Case 3: A 27-year-old gravida 2, para 1 developed an acute abdomen at 25 weeks gestation. A clinical diagnosis of acute pancreatitis was suspected on the basis of history and examination. Biochemistry confirmed acute pancreatitis along with hypercalcemia *(Table I).* An ultrasound of the neck demonstrated an enlarged left inferior parathyroid gland. The patient underwent para-thyroidectomy under general anaesthesia at 30 weeks gestation

TABLE I–*Maternal Serum Biochemistry at Diagnosis.*

Serum biochemistry	Case 1	Case 2	Case 3	Normal
Calcium (mg/dl)	13.4	11.7	11.9	9-11
Phosphate (mg/dl)	2.7	2.9	3.1	2.5-4.5
Alkaline phosphatase (IU/L)	16	528	28	21-85
Creatinine (mg/dl)	0.6	0.8	0.65	0.8-1.5
Albumin (g/dl)	3.6	3.7	3.9	3.5-5.2
Parathormone (ng/dl)	71	50.8	326	0-27

TABLE II– *Maternal and Neonatal Serum Calcium Levels (mg/dl).*

Serum calcium	Case 1	Case 2	Case 3
Mother: Pre-operative	11.3	11.5	11.2
Post-operative			
12 hours	8.1	6.8	8.8
24 hours	8.5	8.5	8.4
48 hours	7.8	8.1	8.0
7 days	9.3	8.9	9.0
During labour	9.6	9.0	9.3
Cord blood	9.7	9.5	9.0
Infant:			
12 hours	9.5	9.1	8.8
24 hours	8.2	8.8	8.4
48 hours	7.8	9.0	8.6
72 hours	9.4	9.1	9.3
7 days	9.6	9.9	9.0

There were no post-operative complications and serum calcium levels were within normal limits *(Table II).* She delivered a healthy female child vaginally at 38 weeks of gestation. The infant's serum calcium levels are shown in *Table I.* The child was kept on oral calcium supplements and is normal at one year of age.

Discussion

The above three cases illustrate the varied symptomatology in hyperparathyroidism. The first case presented with non-specific symptoms, the second with bone pain and swelling and the third as an acute abdomen. In Case 1, it was nephrocalcinosis which prompted us to do serum calcium levels, in case 2, they were done after the histopathology report of the bone tumor and in Case 3, they were done as a part of a routine investigation for acute pancreatitis. Diagnosis was confirmed by parathyroid hormone assays, detection of parathyroid swellings on cervical ultrasound and histopathology. In a review of 159 pregnancies(13), maternal problems associated with hyperparathyroidism included bone disease in 24, renal disease in 34, hypertension in 6, pre-eclampsia in 2, pancreatitis in 2 and parathyroid crisis in 4. Of these 159 pregnancies only 53% resulted in normal infants at term. Neonatal tetany occurred in 22%, neonatal death following tetany in 3% and permanent hypoparathyroidism in 0.6%.

Parathyroidectomy is the only definitive treatment for primary hyperparathyroidism, as it provides prompt resolution of hypercalcemia and its potential complications. Kristoffersson *et al* (14) reviewed 102 pregnancies in hyperparathyroid mothers, 23 of whom were operated during pregnancy and 79 were not (the gestation at the time of surgery is not mentioned). In the non-surgical group there was a 16% incidence of perinatal death and a 53% incidence of neonatal complications whereas in the surgical group it was 9% and 2%, respectively. Second trimester is recommended as the optimum time for surgery, after all the fetal systems have developed (1,6), and the fetus has time to allow for recovery of his own parathyroids, thus reducing the risk of neonatal tetany. Also, the uterus is more capable of effective labor during third trimester; therefore, surgical exploration appears least hazardous during second trimester (4). Available literature on parathyroidectomy in the third trimester though sparse does not mention any increased risk of maternal or neonatal

complications(13,15). All our patients had third trimester surgeries, under regional anesthesia and there was no maternal or neonatal morbidity or mortality.

Until recently, it was accepted that maternal serum calcium concentration fell during pregnancy and this produced a state of secondary hyperparathyroidism(16). However, it has been shown that although total calcium concentrations fall, albumin-adjusted calcium concentration rises as pregnancy progresses(17). All our patients were asymptomatic before pregnancy and became symptomatic only in the second trimester raising a possibility of pregnancy unmasking latent hyperparathyroidism.

Hyperparathyroidism is associated with fetal wastage as well as maternal and neonatal morbidity and many cases are missed due to nonspecific symptoms and variable presentation. It may be worthwhile to do serum calcium levels routinely in all pregnant women. Parathyroidectomy should be performed soon after diagnosis even in the third trimester.

REFERENCES

1. Lowe DK, Orwoll ES, McClung MR, Cawthon ML, Peterson CG. Hyperparathyroidism and pregnancy. Am J Surg 1983,145: 611-164.
2. Heath H, Hodgson SF, Kennedy MA. Primary hyperparathyroidism: Incidence, morbidity and potential economic impact in a community.N Engl J Med 1980, 302: 189-193.
3. Ludwig GD. Hyperparathyroidism in relation to pregnancy. N Engl J Med 1962, 267: 637-642.
4. Delmonico FL, Neer RM, Cosimi AB, Barnes AB, Russell PS. Hyperparathyroidism during pregnancy. Am J Surg 1976,131: 328-337.
5. Mansberger MD, Mansberger AR Jr. Hyper-parathyroidism and pregnancy. J Med Assoc Ga 1988, *77:* 309-312.
6. Gelister JSK, Sanderson JD, Chappie CR, *et al.* Management of hyperparathyroidism in pregnancy. Br J Surg 1989, 76 1207-1280.
7. Higgins RV, Hisley JC. Primary hyperparathyroidism in pregnancy. J Reprod Med 1988, 33: 726-729.
8. Rajala B, Rafat A, Allasi A. Acute pancreatitis and primary hyperparathyroidism in pregnancy: Treatment of hypercalcemia with magnesium sulfate. Obstet Gynecol 1987, 70: 461-462.
9. Patterson R. Hyperparathyroidism in pregnancy. Obstet Gynecol 1987, 70: 457-459.
10. Lopez JM, Fardella CB. Primary hyperparathyroidism: Changes on bio chemical and hormonal profile related to pregnancy. J Endocrinol Invest 1989, 12: 127-129.
11. Wilkinson H, Poon P, Stott A. Hyperparathyroidism in pregnancy: Three case reports. Ann Clin Biochem 1992,29: 467-470.
12. Ammann P, Won O, Gast J, *et al.* Alteration of calcium and phosphate metabolism in primary hyperparathyrqidism in pregnancy. Acta Obstet Gynecol Scand 1993, 72: 488-492.
13. Shangold MM, Dor N, Welt SI, *et al* Hyperparathyroidism and pregnancy: A review. Obstet Gynecol Surv 1982, 37: 217-228.
14. Kristoffersson A, Dahlgren S, Lithner F, Jarhult J. Primary hyperparathyroidism in pregnancy. Surgery 1984, 97: 326-330.
15. Wilkinson H, Poon P, Stott A. Hyperparathyroidism in pregnancy: Three case reports. Ann Clin Biochem 1992, 25. 467-470.
16. Pitkin RM. Calcium metabolsim in pregnancy and the perinatal period: A review: Am J Obstet Gynecol 1985,151: 99-109.
17. Payne RB, Little AJ, Evans RT. Albumin-adjusted calcium concentration in serum increases during normal pregnancy. Clin Chem 1990, 36:142-144.