Hypercalcaemia in Pregnancy

A Case Report

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SUMMARY

A case of hypercalcaemia in a pregnant patient on substitution therapy for hypoparathyroidism is reported. The clinical picture included transient cerebral disturbances, acute pancreatitis and persistent partial blindness. Calcium metabolism in pregnancy is discussed, and a possible mechanism for the sequence of events is postulated. The relevant literature is reviewed.


The numerous causes of hypercalcaemia include hyperparathyroidism, vitamin D poisoning and hyperthyroidism. Clinical manifestations include neuromuscular, cardiovascular, renal and gastro-intestinal aberrations. Pancreatitis, the most serious gastro-intestinal complication, is present in 7% of cases, but pancreatic encephalopathy is extremely rare. Ocular involvement has not yet been described.

CASE REPORT

A 28-year-old White woman, para 1, gravida 2, was transferred to the H. F. Verwoerd Hospital because she had become comatose a few hours previously. She was about 28 weeks pregnant.

According to the history obtained from the referring doctor she had undergone a total thyroidectomy for hyperparathyroidism in 1977. Because of postoperative hypoparathyroidism, the patient had been receiving a calcium preparation, dihydrotachysterol, and thyroxine as substitution therapy since then.

Her previous pregnancy and labour 2 years before thyroidectomy had been uneventful and she had given birth to a normal infant who weighed 3,450 g. The present pregnancy had apparently progressed satisfactorily until signs of mild pre-eclampsia (blood pressure 140/100 mmHg) developed at 26 weeks of gestation. A thiazide diuretic was prescribed, without effect. The patient was admitted to hospital but became comatose the next day and was transferred to our unit. According to additional information received from her husband she had been complaining of weariness, loss of appetite, vomiting, diarrhoea, weight loss and headache for 1 week before admission.

On physical examination the patient was comatose. The blood pressure was 130/90 mmHg, and the pulse rate and temperature were normal. Abdominal palpation revealed a normal pregnancy of 28 weeks' duration. Tenderness, which seemed to rouse the patient from her coma, was elicited in the right epigastrium. There was a generalized increase in muscle tone, with mild neck stiffness. The reflexes were brisk and Babinski's sign was positive. Both pupils were equal and reacted to light.

Cerebrospinal fluid analysis, blood sugar values and thyroid function were within normal limits. Marked hypercalcaemia with a serum calcium level of 5.0 mmol/l (normal 2.3 - 2.7 mmol/l) was present. The serum urea level of 12.7 mmol/l (normal 3.0 - 7.5 mmol/l) and serum creatinine level of 290 mmol/l (normal 60 - 150 mmol/l) were also markedly raised. The serum amylase level was 6,272 U/l (normal 100 - 310 U/l) and the urinary amylase level was 11,709 U/l (normal < 1,500 U/l).

A diagnosis of hypercalcaemia with acute pancreatitis in pregnancy was made. Shortly after transfer to the intensive care unit the patient developed pneumonia due to Klebsiella, became hypoxic and required mechanical ventilation. In an attempt to promote the excretion of calcium, intravenous saline and furosemide were administered. The patient was also given dexamethasone, albumin and cephalosporin. The latter was deemed necessary not only to combat the pneumonia but to prevent pancreatic suppuration.

After an initial rise in the serum urea level (maximum 32 mmol/l), renal function returned to normal. The patient also developed transient hypertension (150/100 mmHg) but no proteinuria or oedema. She recovered consciousness after 6 days but was hallucinating, her mental state fluctuating between paranoia and acute dementia. She also complained of impaired vision. Examination of the optic fundi revealed pallor of the optic disc, cotton wool exudates and petechial haemorrhages of the retina. She was found to have limited vision.

The pregnancy progressed satisfactorily, as confirmed by serial tests for serum human placental lactogen and urinary oestriol and repeat sonar examinations. A week before the expected date of delivery the patient went into spontaneous labour and was delivered vaginally of a female infant who weighed 3,355 g. The Apgar score at 1 minute was 9/10.

On physical examination of the infant no abnormalities were found. Thyroid function, renal function and serum calcium levels were normal. The postnatal course was uneventful and mother and baby were discharged home on the 7th day. Both are being followed up. The patient's partial blindness is showing very little improvement.
DISCUSSION

Although acute hypercalcaemia is one of the more common endocrine emergencies, it remains extremely rare in pregnancy. Parathyroid hormone from the parathyroid glands and calcitonin from the parafollicular cells of the thyroid gland play major roles in maintaining the serum calcium level within normal and constant limits. Absence of these hormones prevents automatic regulation of the body's calcium, and substitution therapy has to be instituted. Regular laboratory assessment of the serum calcium values then becomes mandatory. Because of the changes which take place in calcium physiology during pregnancy, a pregnant patient on substitution therapy must be monitored even more carefully. The normal serum calcium level in a non-pregnant patient is 2.3 - 2.7 mmol/l; of this 45.5% is protein-bound and 47.5% ionized. The ionized calcium is the biologically active fraction in the serum, but 7% of the serum calcium is in the form of ultrafilterable complexes basically unimportant in calcium metabolism. The changes which take place in calcium metabolism during normal pregnancy are as follows: There is increased absorption and decreased excretion of calcium. The total serum calcium levels are lower because of relative hypo-albuminaemia of pregnancy. The ionized calcium level and, therefore, the biologically active calcium level in the serum remain constant even though there is increased absorption. In the fetus, parathyroid hormone is suppressed and calcitonin is stimulated by the fetal serum calcium levels which are higher than the maternal levels.

The net result is an increased deposition of calcium in fetal bone. Our patient had no parathyroid or thyroid tissue and was, therefore, devoid of any hormonal feedback and deprived of automatic regulation of serum calcium. A possible mechanism for the hypercalcaemia is as follows: Increased absorption of calcium in pregnancy, which is enhanced by dihydrotachysterol, and decreased excretion of calcium both lead to an increase in the serum calcium values. Dihydrotachysterol increases bone resorption; because the counteracting effect of calcitonin is absent, a greater rise in the serum calcium values results. This effect is potentiated still further by the thiazide diuretic. Since there is less albumin to bind with the calcium, the biologically active calcium in the serum will be increased. Cerebral disturbance due to hypercalcaemia has been well documented. Headache, fatigue, lethargy, apathy, depression, delirium, coma, neurotic behaviour, hallucinations, paranoia and generalized muscle weakness are all described. Increasing sleepiness, weakness and personality changes in a hypercalcaemic patient could be warning signs of an imminent hypercalcaemic crisis. It is important that the diagnosis is made as soon as possible and immediate treatment is instituted, since the mortality rate in these cases is higher than 50%. The increased serum calcium level gives rise to nausea and polyuria, which in turn leads to dehydration and renal failure. Severe muscular weakness, apathy, depression, malaise and fatigue may follow. Delirium and hallucinations sometimes feature prominently and may be accompanied by focal or general convulsions with cerebrovascular thrombosis or haemorrhage. Terminally the patient develops hypothermia and circulatory collapse. The differential diagnosis includes cerebral arteriosclerosis, brain tumour, subdural haematoma, cerebral haemorrhage, alcoholic psychosis and hypertensive encephalopathy.

Pancreatitis as a complication of hypercalcaemia is well documented, and is thought to be due to the intrapancreatic activation of trypsinogen by the increased concentration of calcium ions, leading to acute necrosis of the gland. Chlorothiazides have also been incriminated as causing pancreatitis in pregnant patients.

Pancreatic encephalopathy is an extremely rare complication of acute pancreatitis. The clinical features of pancreatic encephalopathy, which correspond closely to those of hypercalcaemia, include delirium, hallucinations, convulsions, bilateral clonus, and a positive Babinski's sign. There is also a fluctuation between relative normality and profound neurological disturbance.

This case clearly demonstrated that, as always, endocrine disturbances in pregnancy warrant careful monitoring and specialized care to ensure that the delicate endocrine balance is maintained at all times.

REFERENCES