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Case Report

Pregnancy, parathyroids, and a crisis of calcium: unmasking hypercalcemic crises in pregnancy and beyond: a dual case report

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ABSTRACT

Hypercalcemia is a rare complication during pregnancy, but when it occurs, it can lead to significant maternal and fetal morbidity. Primary hyperparathyroidism is the most frequent cause; however, other uncommon mechanisms such as parathyroid hormone-related protein (PTHrP) secretion by uterine fibroids have been described. We presented two cases. The first involved a 36-year-old primigravida at 34 weeks with severe hypercalcemia associated with a large uterine fibroid. Her condition required intensive care, urgent hemodialysis, and emergency cesarean section. Despite intraoperative complications, both mother and infant survived. The second case was a 37-year-old woman at 24 weeks who was found to have hypercalcemia with elevated parathyroid hormone (PTH) levels while hospitalized for pulmonary embolism. She was not a candidate for surgery and was successfully managed with hydration, calcitonin, vitamin D, and cinacalcet, achieving near-normal calcium levels before delivery. Both pregnancies resulted in live infants. Hypercalcemia in pregnancy requires a high index of suspicion and multidisciplinary management. These two cases highlight rare but important clinical scenarios: fibroid-associated humoral hypercalcemia and the use of cinacalcet for refractory primary hyperparathyroidism during pregnancy.

Keywords: Hypercalcemia, Pregnancy, Parathyroid hormone-related protein, Uterine fibroid, Primary hyperparathyroidism, Cinacalcet

INTRODUCTION

Hypercalcemia during pregnancy occurs in approximately 0.03% of women of reproductive age.[1] The severity of complications is directly linked to the level of maternal calcium.[2] Maternal complications include nephrolithiasis, kidney injury, pancreatitis, and pre-eclampsia.[3,4] Additionally, hypercalcemia can lead to significant fetal risks, such as fetal loss.[5,6] The degree of hypercalcemia plays a crucial role in determining the likelihood and severity of these complications. Severe hypercalcemia in pregnancy is uncommon but poses a serious risk to both mother and baby.[1,2] Generally, hypercalcemia during pregnancy can be caused by various pathological conditions. Primary hyperparathyroidism is the most frequent cause.[7] Additional factors contributing to hypercalcemia are hyperthyroidism, immobility, excessive levels of vitamin D or vitamin A, familial hypocalciuric hypercalcemia, diuretic phase of acute renal failure, chronic kidney disease, thiazide diuretics, sarcoidosis or other granulomatous diseases, milk-alkali syndrome, and Addison's disease.[2,8] It is also possible for pregnant women to experience hypercalcemia due to tumors

producing parathyroid hormone-related protein (PTH-rP).[9] It is very uncommon to experience hypercalcemia caused by elevated levels of PTH-rP in the context of benign conditions.[10]

CASE REPORTS

Case 1

A 36-year-old Kenyan woman, primigravida at 34-week spontaneous pregnancy, admitted to our hospital, with a chief complain of recurrent vomiting and epigastric pain. She was diagnosed with uterine fibroid in the initial month of her pregnancy, yet the pregnancy had been without any complications and with smooth progress. She also gives a history of wight loss of about 10 kg, with no alterations in her bowel habit, no hematemesis or malena, and no past episodes of hematuria or passing stones. The patient's medical history was normal except for the fact that she was taking iron tablets.

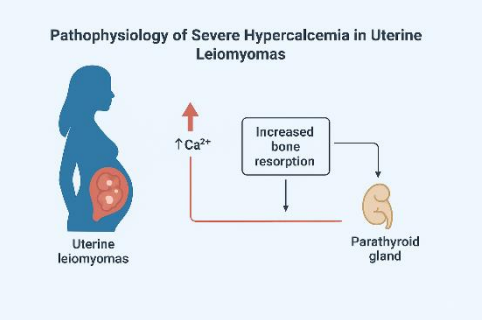

Figure 1: Pathophysiology of severe hypercalcemia in uterine leiomyomas.

Table 1: Dynamic relationship between hypercalcemia, PTH suppression, and post-surgical normalization, along with albumin trends reflecting her nutritional and inflammatory status.

Timelines	Serum calcium (mmol/l)	Phosphorus (mmol/l)	PTH (pg/ml)	Albumin (g/l)	Notes
14 weeks gestation	2.43	—	—	—	Retrospective calcium measurement
34 weeks gestation	4.8	0.8	3	30	Severe hypercalcemia, low PTH, humoral hypercalcemia
Post-fibroid removal	2.34	1.1	155	21	Calcium dropped; PTH rebound post-surgery
1 month postpartum	~2.4–2.5	~1.0	—	~35	Biochemical stabilization
3 months postpartum	~2.4–2.5	~1.0	—	~40	Stable
6 months postpartum	~2.4–2.5	~1.0	—	~42	Maintained within normal range

Table 2: Maternal interventions and timeline.

Time/gestation/ postpartum	Intervention/management	Rationale/notes	Maternal response
Admission (34 weeks)	IV normal saline 250 ml/h	Correct dehydration, hypercalcemia support	Urine output monitored; partial calcium decrease
Admission	Intramuscular calcitonin	Hypercalcemia management	Limited effect
ICU	Hemodialysis prior to emergency C-section	Elevated calcium, decreased urine output	Calcium controlled
Emergency C-section	Delivery + removal of uterine masses	Ruptured membranes + uterine fibroid	Baby delivered successfully
Postoperative	Blood transfusions + broad-spectrum antibiotics	Management of hypotension & septic shock	Patient stabilized
Postoperative	Intensive physiotherapy	Muscle weakness and stiffness	Gradual improvement

Table 3: Maternal and neonatal outcomes.

Parameters	Maternal outcome	Neonatal outcome
Delivery	Emergency C-section; removal of 30×25×15 cm fibroids	Female baby, 2.9 kg, healthy
Calcium levels	Post-op 2.34 mmol/l; normalized within 6 months	N/A

Continued.

Parameters	Maternal outcome	Neonatal outcome
PTH	Post-op 155 pg/ml	N/A
Postoperative complications	Sepsis, septic shock, hypotension, hypoxic brain injury	None
Imaging	Brain infarcts & diffuse ischemic changes post-op	N/A
Long-term follow-up	Recovered with physiotherapy; stable calcium	N/A

Upon inspection, she appeared unwell, severely dehydrated and drowsy. She had a blood pressure of 126/76 mmHg, a pulse rate of 94 /min, a respiratory rate of 30/min, and a temperature of 36.6°C; there were no signs of lymphadenopathy, thyromegaly, or edema. The abdominal exam revealed a uterus size equivalent to 40 weeks and tenderness in the epigastric region. Examination of the nervous system revealed drowsy and hypotonic lady with brisk deep tendon reflexes. There was no clear neurological sign that stood out. The planter's reflexes were downward. There were no notable findings in the chest and cardiovascular systems.

Based on these laboratory findings, the possible diagnosis was humoral hypercalcemia of benignancy (uterine fibroid). PTH-rP is the primary mediator that causes hypercalcemia. However, we did not check for the PTH-rP level because of lack of facilities.

The initial results showed: hemoglobin (Hb) 8.7 g/dl, WBCs 7000 µl-1, platelets 445 000 µl-1; and ESR 109 mm/h. Toxic granulation of white blood cells was observed in the peripheral blood smear. Blood chemistry: BUN at 4.4 mmol/l, creatinine at 59 µmol/l, HCO_3 at 22 mmol/l, Na at 138 mmol/l, Ca at 4.8 mmol/l (within normal range of 2.1-2.6), uric acid at 508 µmol/l, lactic acid at 1.2 mmol/l, and phosphorous at 0.8 mmol/l. The results of the HIV tests came back as negative. A retrospective measurement of calcium at 14 weeks' gestation was obtained at 2.43 mmol/l. Liver function test results: ALT level was 4 u/l, AST level was 11 u/l, ALP level was 150 u/l, total protein level was 72 g/l, and albumen level was 30 g/l. Cholesterol level was 4.05 mmol/l and triglyceride level was 3.59 mmol/l in the lipid profile. Study on hormones: PTH levels at 3 pg/ml (normal range: 15-65), TSH levels at 0.68 mIU/l (normal range: 0.45-4.5), free thyroxin at 16.6 pmol/l (normal range: 9-20), cortisol at 1849 nmol/l, and vitamin D at 15 ng/ml (normal range: 30-80). Serum protein electrophoresis and serum angiotensin-converting enzyme levels were within normal range.

With the internist's approval, the patient received a normal saline infusion at a rate of 250 ml/h while closely monitoring her urine output, in addition to receiving intramuscular calcitonin, before being moved to the medical intensive care unit.

According to these lab results, the likely diagnosis was benign humoral hypercalcemia (uterine fibroid). PTH-rP is the main factor responsible for inducing hypercalcemia. Nevertheless, we omitted the PTH-rP level as was not available in the hospital.

In the ICU, the patient experienced a ruptured membrane, resulting in the need for an emergency cesarean section even though calcium levels were still elevated. Due to hypercalcemia and decrease in urine output with an increase in serum creatinine levels, the nephrologist was asked for prompt hemodialysis prior to the surgery. Although the surgery got complicated with severe blood loss resulting in significant hypotension which was managed with blood and blood products transfusion, despite the successful delivery of a 2.9 kg baby girl and removal of uterine masses measuring a total of 30×25×15 cm. The masses were sent for further histopathological assessment and reported for leiomyoma with calcifications but no evidence of malignancy. The postoperative clinical course was further complicated by sepsis and septic shock, which required vasopressors and broad-spectrum antibiotics.

The results of the postoperative lab tests showed: calcium 2.34 mmol/l, phosphorus 1.1 mmol/l, BUN 6.2 mmol/l, Cr 75 mmol/l, Na 143 mmol/l, K 4.2 mmol/l, HCO3 16 mEq/l, chloride 113 mEq/l, albumin 21 g/l, serum lactate 5.19, serum PTH 155 pg/ml, serum amylase 88 u/l, serum lipase 73 u/l; Hb 5.8 g/dl, platelets 125 000 µl1. The chest and pelvis CT scan did not reveal any signs of a mass lesion or organ enlargement. An MRI of the brain was conducted due to a decline in consciousness level, revealing infarcts in the right cerebellum, lentiform nucleus on both sides, and cortical regions in the frontal, parietal, and occipital lobes. MRA displayed signs of vasospasm in the internal carotid, middle, and anterior carotid arteries, indicating widespread diffuse ischemic changes secondary to hypoxic insult. Following that, her health started to get better, but she needed intensive physiotherapy due to muscle weakness and stiffness throughout her body. The patient was sent home with a diagnosis of humoral hypercalcemia linked to a uterine fibroid. Serum calcium levels stayed within normal limits for the following 6 months.

Case 2

A 37-year-old woman was admitted to the Women's hospital at 24 weeks gestation with shortness of breath. Her working diagnosis was pulmonary embolism, as she had a history of recurrent deep venous thrombosis. She was placed on a therapeutic dose of enoxaparin. A routine

blood test during hospitalization revealed hypercalcemia; corrected calcium level was 3.17 mmol/l (reference range, 2.1 to 2.60 mmol/l); PTH was elevated to 168 pg/ml (reference range, 15 to 65 pg/ml), and vitamin D was low at 12 ng/ml. The patient had no symptoms of hypercalcemia. The rest of the work-up is shown in Table 1.

On further questioning, she said that following her last delivery 10 years previously in her home country, her newborn developed severe tetany and required admission to the neonatal intensive care unit, where he was treated with intravenous (IV) calcium for a few weeks and then treated with oral calcium until he was 2 years of age. Medical records from the previous pregnancy were not available. She denied a personal history of fractures or kidney stones or family history of hypercalcemia. She did not recall that she had received any further investigations, and no follow-up was arranged for her.

Table: 4 Timeline of clinical events and interventions.

Time point (gestation/postpartum)	Clinical event/ finding	Intervention/ management	Maternal outcome	Fetal/neonatal outcome
24 weeks	Admitted with SOB; hypercalcemia	IV fluids, calcitonin	Hypercalcemia persisted	N/A
26 weeks	Continued high calcium	Vitamin D2 supplementation	No symptoms; monitored	N/A
32 weeks	Calcium still elevated	Cinacalcet started	Calcium started decreasing	N/A
36 weeks	Calcium normalized (<2.60 mmol/l)	Continued cinacalcet	Stable	N/A
37 weeks	Spontaneous labor; emergency C-section	Multidisciplinary management	Healthy post-op	Neonate born; calcium 2.94 mmol/l
Day 4 post-delivery	Neonatal nadir calcium	Monitoring & breastfeeding support	N/A	2.46 mmol/l; stable afterwards
10 months	Follow-up	Routine monitoring	Healthy	Calcium stable at 2.49–2.53 mmol/l

Table: 5 Maternal medication and dosage.

Medication/ therapy	Dose and frequency	Duration	Indication	Response/outcome
IV fluids	As per protocol	Initial hospitalization	Hypercalcemia	Calcium persisted
Calcitonin	400 IU IM twice/day	~1 week	Hypercalcemia	No significant drop
Vitamin D2	1,000 IU/day	Ongoing	Vitamin D deficiency	Corrected deficiency
Cinacalcet	15 → 15 mg twice/day	32-37 weeks	Hypercalcemia management	Calcium <2.60 mmol/l at delivery

Table 6: Maternal and neonatal outcome summary table.

Parameters	Maternal outcome	Neonatal outcome
Delivery	Emergency cesarean section	Born at 37 weeks; healthy
Calcium levels	Normalized with therapy	Mild transient hypercalcemia; stable afterwards
PTH/vitamin D	PTH elevated; Vitamin D corrected	N/A
Complications	None	No hypocalcemia or adverse events
Follow-up	Stable	Calcium stable at 10 months

Table 7: Comparison of case 1 and case 2.

Features/parameters	Case 1	Case 2
Maternal age (in years)	36	37
Gravida/ parity	Primigravida	Not specified

Continued.

Features/parameters	Case 1	Case 2
Gestational age at Presentation	34 weeks	24 weeks
Chief complaint/ presentation	Recurrent vomiting, epigastric pain, dehydration	Shortness of breath; incidental hypercalcemia
Past history	Uterine fibroid; no fractures, stones	Recurrent DVT; prior neonatal tetany
Etiology of hypercalcemia	Humoral hypercalcemia of benignancy (likely PTHrP from fibroid)	Primary hyperparathyroidism
Initial corrected calcium	4.8 mmol/l	3.17 mmol/l
PTH level at presentation	3 pg/ml (suppressed)	168 pg/ml (elevated)
Vitamin D	15 ng/ml (deficient)	12 ng/ml (deficient)
Initial management	IV fluids, calcitonin, hemodialysis	IV fluids, calcitonin, vitamin D, cinacalcet
Definitive management/ surgery	Emergency C-section + fibroid removal	Conservative; cinacalcet; elective C-section
Maternal complications	Sepsis, hypotension, hypoxic brain injury	None reported
Neonatal outcome	Female baby 2.9 kg, healthy	Baby monitored; transient mild hypercalcemia; stable at 10 months
Follow-up	Maternal calcium normalized at 6 months	Maternal calcium normalized; neonatal calcium stable

During her current pregnancy, hypercalcemia was initially treated with IV fluids and calcitonin 400 IU intramuscularly twice per day, but the corrected calcium levels were unchanged. Due to concomitant vitamin D deficiency, she was commenced on vitamin D2 1,000 IU/day based on recent recommendations for nonpregnant females. Surgical consultation was obtained, and neck ultrasonography did not localize a parathyroid adenoma. She was at considerable high risk to undergo neck exploration. As the level of calcium during the last pregnancy was not known, the aim was to keep the corrected calcium levels as normal as possible to avoid neonatal hypocalcemia. The possibility of treatment with cinacalcet was discussed with the patient. The patient was counselled about the potential benefits of cinacalcet based on the available case reports and told that cinacalcet was not approved during pregnancy. After discussing the pros and cons of treatment, the patient started on oral cinacalcet 15 mg once daily, which was later increased to 15 mg twice daily. By 36 weeks gestation, corrected calcium levels were down to <2.60 mmol/l. Elective caesarean section was planned at 38 weeks gestation, yet she presented at 37 weeks with labor pains. Her corrected calcium level was 2.57 mmol/l. The patient underwent emergency caesarean section, which was attended by a neonatologist.

The immediate corrected calcium level of the neonate was 2.94 mmol/l (reference range, 2.19 to 2.88 mmol/l). The newborn's calcium levels were monitored twice daily for 5 days, reaching a nadir of 2.46 mmol/l on day 4 postdelivery. The child was breastfed, and the serum calcium remained steady between 2.49 and 2.53 mmol/l until the last available follow-up at 10 months of age.

The Table 5 summarizes the chronological sequence of events, treatments, and outcomes. It's particularly useful for pregnancy-related cases where maternal and fetal events need to be clearly linked.

The Table 6 focuses on therapeutic interventions with dose, duration, and rationale, which is useful for readers and reviewers.

A concise summary table that highlights key outcomes, especially for pregnancy-related case reports.

DISCUSSION

Hypercalcemia during pregnancy is rare but poses significant risks to both mother and fetus.[1,2] Primary hyperparathyroidism is the most common cause, but in some cases, benign tumors or excessive PTH-rP production may be implicated.[7,10] Humoral hypercalcemia of benignancy has been reported in association with uterine leiomyomas.[8] PTH-rP, identified by Moseley et al. in 1987, plays an essential role in calcium regulation and may be expressed in reproductive tissues, contributing to smooth muscle relaxation and myometrial activity.[7,9]

In the first case, hypercalcemia was attributed to humoral hypercalcemia associated with uterine fibroids. Other causes such as hypervitaminosis, granulomatous disease, and primary hyperparathyroidism were excluded.[2,8] The patient's management required multidisciplinary coordination involving obstetrics, nephrology, and critical care. Intravenous hydration, calcitonin, and hemodialysis were effective in stabilizing calcium before delivery.[11,12]

In the second case, the patient had primary hyperparathyroidism (PHPT) diagnosed during pregnancy. When surgical management was contraindicated, cinacalcet was successfully used to control calcium levels.[16,18] Although evidence for cinacalcet use in pregnancy remains limited, several reports have shown favourable maternal and neonatal outcomes when surgery is not feasible.[15,18]

Hypercalcemia can cause severe maternal complications such as pancreatitis, nephrolithiasis, and renal failure, as well as fetal loss and neonatal hypocalcemia.[3,6] Managing these cases requires early detection, close biochemical monitoring, and individualized therapeutic decisions.

CONCLUSION

In conclusion, hypercalcemia during pregnancy, though rare, presents a diagnostic and therapeutic challenge requiring a high index of suspicion and coordinated multidisciplinary care. Together, these two cases demonstrate that severe maternal hypercalcemia during pregnancy may arise from distinctly different but equally critical mechanisms, humoral hypercalcemia associated with uterine fibroids and primary hyperparathyroidism, and both require high clinical suspicion, rapid evaluation, and tailored management to prevent maternal and neonatal complications. By highlighting a rare benign cause of PTH-rP-mediated hypercalcemia and illustrating the cautious yet effective use of cinacalcet when surgery is not feasible for PHPT, this report broadens current understanding of the differential diagnosis, biochemical interpretation, and therapeutic approaches for hypercalcemia in pregnancy. These insights add important clinical evidence to a sparsely documented area and underscore the necessity for individualized, multidisciplinary strategies to ensure optimal outcomes for both mother and fetus.

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