Submitted: 14.02.2024
Accepted: 26.02.2024
Early publication date: 06.05.2024

Endokrynologia Polska
DOI: 10.5603/ep.99376
ISSN 0423–104X, e-ISSN 2299–8306
Volume/Tom 75; Number/Numer 3/2024

Acute pancreatitis associated with primary hyperparathyroidism during pregnancy

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Key words: *acute pancreatitis; primary hyperparathyroidism; pregnancy; cinacalcet; parathyroidectomy*

Primary hyperparathyroidism (PHPT) during pregnancy is rarely reported (0.05–1%), but it is the most common cause of gestational hypercalcaemia [1]. PHPT might be a preventable cause of maternal and foetal morbidity and mortality. The most common cause of PHPT is benign, solitary parathyroid tumour (85%) [2]. The clinical presentation of PHPT in pregnancy varies. Pancreatitis is a rare manifestation of PHPT, but it can occur in 10% of all cases [3].

A 30-year-old in second pregnancy nulliparous woman was admitted at the 29th gestational week with upper left quadrant epigastric acute pain and nausea with vomiting. The pregnancy had been complicated by acute pancreatitis (AP) at the 17th gestation week and pregnancy-induced hypertension. Her first pregnancy ended in a spontaneous miscarriage in the first trimester 2 years before without any medical investigation.

On admission the patient's vital signs were stable, but physical examination revealed positive Blumberg sign in the epigastric area and reduced bowel sounds. The gynaecological examination did not show any abnormalities and confirmed the foetus' well-being. Abdominal ultrasound showed the pancreas with blurred outlines and bilateral nephrocalcinosis.

Oxycodone was administered for pain management. The laboratory results pointed out a 16-fold increase in serum alpha-amylase and a 30-fold increase lipase. Normocytic anaemia (9.2 g/dL — N: 11.5–15 g/dL), increased inflammatory serum markers (white blood cells 26 k/uL — N: 4–10 k/uL; C-reactive protein 57 mg/dL — N: < 4 mg/dL), mild hyponatraemia (134 mmol/L — N: 136–145 mmol/L), parathormone-dependent hypercalcaemia (total calcium level 14.6 mg/dL — N: 8.6–10 mg/dL), and hypophosphataemia (2.09 mg/dL — N: 2.5–4.5 mg/dL) were noted. Moreover, hypertriglyceridaemia (335 mg/dL — N: < 150 mg/dL) and hypercreatinaemia (1.69 mg/dL — N: 0.51–0.95 mg/dL) with reduced glomerular filtration rate (40 ml/min) were observed. The patient was diagnosed with severe AP due to PTH-dependent hypercalcaemia.

Initially, conservative treatment was introduced with parenteral nutrition, intravenous hydration, and cinacalcet (60 mg/day, 30 mg per os in every 12 h). Additionally, the patient was given heparin, antibiotics, corticosteroids to accelerate foetal lung maturation and to reduce the absorption of calcium from the gastrointestinal tract and IV magnesium sulphate (4 g/day; 2 g in every 12 h). In the following days inflammatory markers and the levels of lipase and amylase decreased, while the serum levels of PTH and calcium remained at high levels (Fig. 1A–B).

The haemoglobin level was decreasing, and differential diagnosis was performed revealing no symptoms of active bleeding or haemolysis. To manage anaemia level 6 units of packed red blood cells were transfused and an erythropoietin analogue was given.

The neck ultrasound highlighted a structure measuring 12 × 10 × 15 mm in the parathyroid area, suggesting adenoma. Mediastinum magnetic resonance imaging (MRI) did not identify any pathological changes. On the 17th day of hospitalisation, due to the risk of hypercalcaemic crisis and unsatisfactory results of conservation treatment approach, the patent was schedule for surgical intervention — the left lower parathyroid gland was completely removed. Intraoperative measurement of PTH concentration in blood

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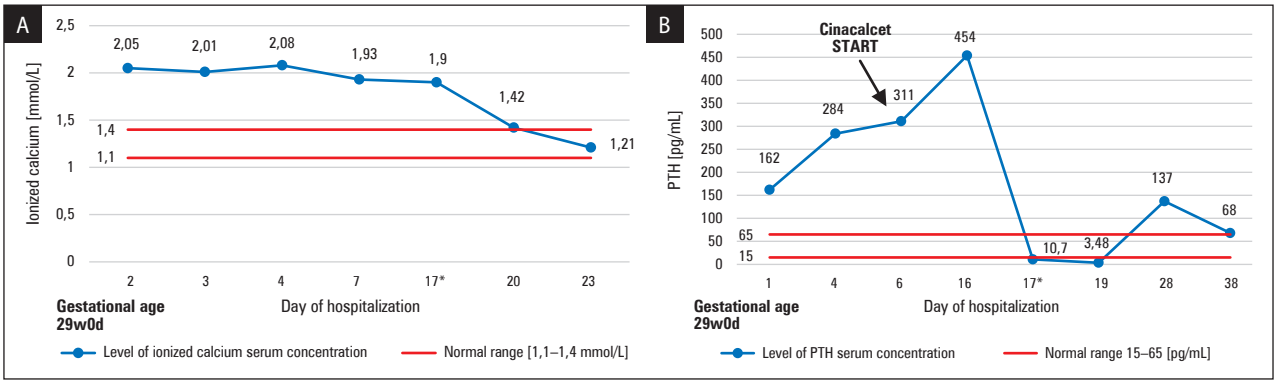

Figure 1. A. *Ionized calcium serum concentration [normal range 1.1–1.4 mmol/L];* **B.** *Parathormone (PTH) serum concentration [normal range 15–65 pg/mL]. *day of surgery*

serum showed a significant decrease after the partial parathyroidectomy (PTX). Parathyroid adenoma was confirmed in histopathological examination. The postoperative period was uncomplicated.

In the following postoperative days, increasing PTH values were obtained, with a plateau phase and a subsequent decline to a normal range. In the 34th gestational week, due to intraamniotic infection (meeting Gibb's criteria), an emergency C-section was performed. A male infant was delivered, weighing 2580 g with Apgar score of 7/7 points. No hypocalcaemic disorders were noted in the neonate.

Gestational PHPT remains underdiagnosed and misleading, and clinical knowledge in this area is based on few case descriptions and retrospective studies [4]. A similar approach should be taken in cases of unexplained history of miscarriage, pancreatitis, low-trauma bone fracture, peptic ulcer, and first trimester hypertension.

Diagnostics and treatment approaches are limited and require individual risk-benefit assessment. The management of gestational PHPT is challenging because some treatments are contraindicated in pregnancy or are not evidenced-based [4]. The neck USG should be performed to localize the lesion [4].

The management of PHPT includes conservative treatment and surgery (if non-responsive to medical treatment). There is increasing evidence supporting the use of surgery regardless of the stage of pregnancy [4]. According to the guidance, the second trimester is the preferable time to perform the surgery [4]. PTX should not be postponed to the third trimester because prolonged exposition to hypercalcaemia increases the risk of neonatal hypocalcaemia, tetanus, foetal growth restriction, and foetal mortality [4]. As far as maternal adverse outcomes are concerned, hypertension seems to be the most important issue. Women with PHPT may develop eclampsia, preeclampsia, and HELLP syndrome [4]; thus, proper diagnosis is crucial to monitor the patient closely and to treat the disease accordingly and effectively.

In the case of a pregnant patient presenting upper left quadrant epigastric acute pain with concomitant hyperemesis gravidarum and unusual symptomatology, the serum calcium level should be assessed because the diagnosis of PHPT may change the treatment modality of the mother and neonate. In some cases, when conservative management fails, surgical intervention is required, causing no adverse event for the mother or her child. The most frequent serious complications of uncontrolled gestational hypercalcaemia that can arise as a result of maternal hypercalcaemia are neonatal tetany, stillbirth, and abortion.

Ethics statement

This case report was conducted in accordance with the Declaration of Helsinki.

Author contributions

The author confirms sole responsibility for the following: case report conception, discussion and vignette preparation.

Conflict of interest

Authors declare no conflict of interest.

Funding

None declared.

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