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Treatment of parathormone-dependent hypercalcaemia in the third-trimester of pregnancy

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Primary hyperparathyroidism (PHPT) in pregnancy is an endocrine disorder causing PTH-dependent hypercalcaemia (HDPHT), with a prevalence of 0.15–0.4% in the general population [1]. Disease symptoms remain polysymptomatic and non-specific such as nausea, weakness, anorexia, constipation (36%), and muscle aches, fatigue, and mood swings, which can be confused with common discomfort in pregnancy. Organ symptoms may present: kidney stones (24–36%), radiographic bone disease (13–19%), pancreatitis (7–13%), pregnancy vomiting, muscle weakness, hypertension, eclampsia, pre-eclampsia, confusion, and function-critical hypercalcaemic breakthrough, but 25% may be asymptomatic [2].

A 26-year-old Caucasian pregnant woman in the third pregnancy after 2 natural deliveries in 31 w 1 d, body mass index (BMI) 29.3 kg/m², blood pressure (BP) 120/80 mm Hg, heart rate 84 /min was admitted with symptoms of renal colic, nausea, weakness, constipation, and stenocardia. Electrocardiogram (ECG) and low troponin levels ruled out myocardial ischaemia. Abdominal and Doppler ultrasound imaging (USG) showed no pathological changes in the abdomen, gastrointestinal tract, or urinary tract or signs of thrombosis in the vessels of lower extremities. The thyroid gland was enlarged, cohesive, and asymmetrical, with lobes as follows: right 18 × 20 × 54 mm, left 16 × 15 × 52 mm, isthmus 2.3 mm. Lower pole of right lobe hypoechoic structure 14 × 12 × 7 mm, elasticity contrast index (ECI) — 0.32, and vascularisation II/III°. Laboratory tests indicated high levels of parathyroid hormone (PTH) — 179.3 pg/mL, ionic calcium (iCa) 1.82 mmol/L with reduced values of thyroid-stimulating hormone (TSH) — 0.031 uIU/mL, es-

timated glomerular filtration rate (eGFR) — 40.0 mL/min, and urine-specific gravity 1001 g/L.

Prenatal status on admission: USG estimated foetal weight (EFW) 1435 g — 7th percentile — female, amniotic fluid index (AFI) — 12 cm, Doppler umbilical artery pulsation index (UA-PI) 96th percentile — pathological, cerebroplacental ratio (CPR) — 6th percentile — normal, mid cerebral artery (McA) PI — 15th percentile — normal, mean uterine artery (UtA) PI — 96th percentile — pathological. The mentioned variables led to a diagnosis of foetal growth restriction (FGR) stage 1; cervical length — 3.0 cm. Cardiotocography confirmed foetal well-being. Uterine contractility: base tension 20 mm Hg, uncoordinated contraction to 50 mm Hg.

Conservative treatment included forced diuresis administering 1500 mL of crystalloids and 1500 mL of oral fluid therapy for 24 hours, and diuretics. After 7 days, there was no improvement in subjective well-being, there was no full relaxation of the uterine muscle requiring tocolytic therapy with a decrease in PTH 22.0 ug/mL and eGFR 35.0 mL/min, as well as persistent hypercalcaemia — 1.63 mmol/L. USG shown no significant foetal weight gain — 1550 g — 5 FGR 1. At 32 w 1 d, due to persistent hypercalcaemia and lack of foetal growth, a surgical parathyroidectomy was performed removing a 1-cm diameter adenoma of the right thyroid lobe. Full normalisation of the pregnant woman's condition and laboratory parameters occurred after 7 days. In the further course of pregnancy, she received supplementation with Vitamin D3 2 µg and calcium 2000 mg/24 h. Fourteen days after parathyroidectomy, a follow-up USG was performed:



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EFW was 1890 g — 22nd percentile — appropriate for gestational age (AGA), doppler Ua PI — 54th percentile — normal, mean UtA — 88th percentile — normal, CPR 30th percentile — normal. CTG: Base FHR 140 bpm, STV 7.9 ms, no contractility present. Neonate was delivered at 38 w 2 d by caesarean section. Weight 3070 g — 57th percentile, Apgar score 10/10, with no signs of hypocalcaemia. Vitamin D3 2 µg and calcium 2000 mg/24 h supplementation was used until termination of lactation. The foetal growth trend is shown in Figure 1. Lab test values were as follows: PTH 53.5 pg/mL; Ca 2.08 mmol/L; iCa 1.16 mmol/L.

Foetal complications in pregnancy affected by PHPT range in severity from recurrent abortions, intrauterine growth delay, polyphagia, and in utero demise to cases of neonatal tetany and even neonatal death due to cardiac arrest. Maternal hypercalcaemia causes obvious foetal parathyroid suppression secondary to an increase in placental calcium flow to the foetus. Under conservative management with diuretics, oral hydration, low calcium diet, and D3 supplementation, pregnancies usually proceed normally with continued mild hypercalcaemia [3]. Increased risk of pregnancy loss is more common when calcium levels exceed 2.85 mmol/L [4]. Gestational parathyroidectomy is an effective treatment for PHPT. The main indication is persistent calcium levels > 2.75 mmol/L in cases of recurrent miscarriages of unknown aetiology and/or to treat foetal or maternal complications due to hypercalcaemia [4]. A study including a comparison of 382 cases compared the results of conservative *vs.* surgical treatment of PTHP,

with 71.7% *vs.* 21.1%, respectively. The probability of complications and/or death after surgery in the second trimester of pregnancy was 4.48% lower compared to surgery in the third trimester of 21.1% [5]. In addition, it was shown that the overall neonatal complication rate of surgically treated patients remained lower than that of conservatively treated patients, at 9.1% *vs.* 38.9%, respectively [5]. Intrauterine growth restriction (IUGR) on the background of hyperparathyroidism is rare; however, a differential diagnosis of unknown cause should always consider the aetiology of PTHP. In our case, the effect of HDPTH on FGR is indicated by the improvement of foetal well-being as early as 14 days after parathyroidectomy, as well as delivery of a healthy newborn with a normal birth weight.

Prompt diagnosis and the inclusion of pharmacological and surgical treatment make it possible to cure the pregnant woman and improve foetal well-being. In cases similar to the one referred to, it is advisable to include surgical treatment, where the benefits far outweigh the potential risks associated with surgery and anaesthesia.

Conflict of interests

The authors declare no conflict of interest

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Author contributions

M.Z. — conception, design, methods, investigations, analysis of data, medical supervision, writing of the manuscript and draft, data curation, data visualisation, translation; A.O. — conception, content supervision, methods, investigations, analysis of data, medical supervision; G.B. — methods, investigations, analysis of data, medical supervision; A.M. — investigations, manuscript draft, analysis of data; A.G. — investigations, manuscript draft, analysis of data; J.G. — conception, content supervision, methods, investigations, medical supervision, analysis of data.

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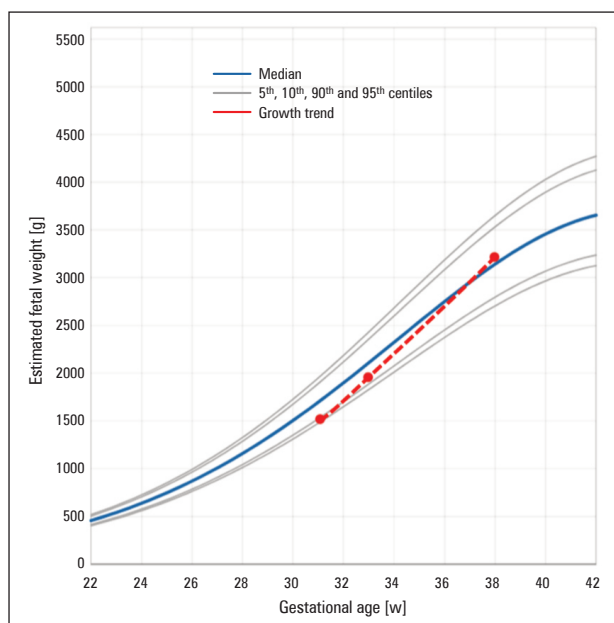


Figure 1. Foetal growth trend in centiles chart: admission day (31 w 1 d), 14 days after parathyroidectomy (33 w 1 d), and on the day of caesarean section (38 w 2 d)