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Primary Hyperparathyroidism and Pregnancy about a Case: Association at Risk for the Mother and Fetus

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Abstract

This case report describes a 30-year-old woman with primary hyperparathyroidism due to a parathyroid adenoma who became pregnant while awaiting surgery. Despite apparently normal total serum calcium during pregnancy, she developed threatened preterm labor and delivered a macrosomia infant at 37 weeks, who subsequently presented with transient neonatal hypercalcemia. The authors review the literature on maternal and neonatal complications associated with hyperparathyroidism in pregnancy and emphasize the importance of early diagnosis and multidisciplinary management.

Keywords

Hypocalcemia, Hypercalcemia, Hyperparathyroidism, Preterm Delivery

1. Introduction

Primary hyperparathyroidism (PHPT) is one of the most frequent endocrine disease in developed countries. It mainly occurs as sporadic cases about 90% - 95% of cases, while only the remaining 5% - 10% is represented by familial inherited parathyroid disorders due to causative mutations in specific target genes [1]. Primary hyperparathyroidism is due to the presence of a benign single parathyroid adenoma in 80% of the cases, to multiple parathyroid adenoma and or multiglandular hyperplasia in 15% - 20% of the cases or to parathyroid carcinoma in only 1% of the cases [2]. The prevalence of primary hyperparathyroidism in the general population is 0.15%. This disease is more common in women, with 25% of cases occurring in women of childbearing age [3]. The combination of hyperparathy-

roidism and pregnancy is a rare condition with an unknown prevalence that requires appropriate and rapid multidisciplinary treatment, as the prognosis can be complicated by significant morbidity and mortality for both mother and child, mainly due to maternal hypercalcemia [4]. We therefore report this case in order to review the literature on obstetric and neonatal complications.

2. Observation

We report the case of a 30-year-old nulligravida patient diagnosed with symptomatic parathyroid adenoma presenting as urinary lithiasis and bone pain in the right shoulder.

Biology: Calcemia = 2.95 mmol/l (2 - 2.6 mmol/l), Phosphatemia = 0.68 mmol/l (0.87 - 1.45 mmol/L), PTH = 144 pg/mL (15 - 65 pg/mL). The cervical ultrasound showed a parathyroid adenoma measuring 2.1 × 1.2 mm in the lower posterior right thyroid lobe (**Figure 1**).

Radiography of the right shoulder revealed osteolysis of the proximal third of the right shoulder and the distal end of the clavicle (**Figure 2**). While awaiting a complete endocrine examination and surgery, she became pregnant with complications of threatened premature delivery at 35 weeks of gestation. The tocolysis used was nifedipine 20 mg per os every 8 hours for 2 days. During her follow-up, her calcium level was normal (86 mg/l) at 35 weeks. She underwent artificial induction of labor at 37 weeks, giving birth to a newborn weighing 4000 g who, at two weeks of age, presented with constipation and hypercalcemia at 109 mg/L, which responded favorably to treatment. One year later, no clinical manifestations have been noted in the child and the mother decided to postpone the surgery for his owns reasons.

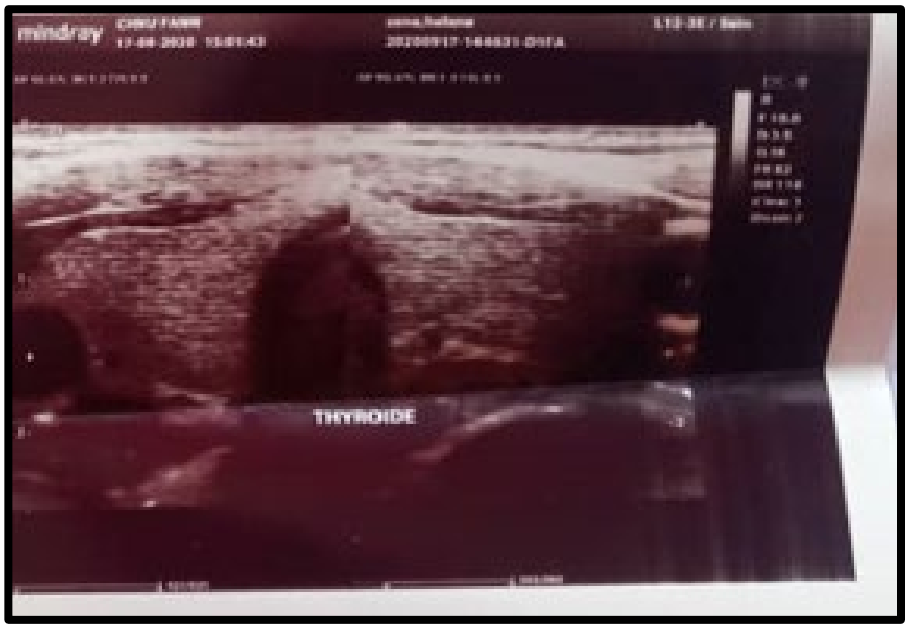

Figure 1. Ultrasound image of a parathyroid adenoma in the right thyroid lobe.

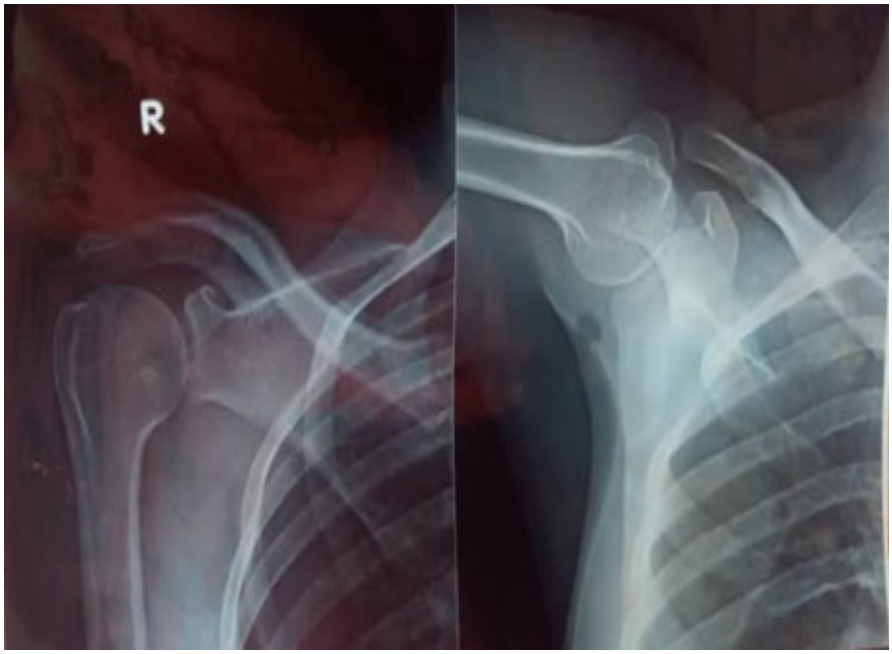

Figure 2. Osteolysis of the proximal third of the humerus and the distal end of the clavicle.

3. Discussion

The rate of maternal complications reaches 14% - 67% of cases, with the most serious complication being hypercalcemic crisis, which requires close monitoring in the postpartum period. Other obstetric complications are also observed, such as acute polyhydramnios or intrauterine growth restriction, preeclampsia, premature delivery, and neonatal death.

The rate of fetal complications can reach 45% - 80% of cases, with neonatal hypocalcemia being the main complication [4] [5]. Our patient presented with a maternal obstetric complication of threatened premature delivery at 35 weeks of gestation that required treatment with tocolysis.

Obstetric complications tend to increase in cases of primary hypercalcemic hyperparathyroidism compared to normocalcemia or hypoparathyroidism. Charbit *et al.* found 44% of complications in case of hypercalcemia compared with 33.3% in normocalcemia and 28.6% in hypoparathyroidism [6]. Norman *et al.* found more common loss pregnancy as calcium levels exceed 11.4 mg/dl (2·85 mmol/l), but can be seen at all elevated calcium levels [7].

During a hypercalcemic and hyperparathyroidism pregnancy, the transplacental passage of calcium leads to significant hypercalcemia in the fetus. As the fetal parathyroid glands are functionally reactive, it is assumed that parathyroid suppression occurs in utero due to high calcium levels. This can lead to neonatal tetany or even permanent neonatal hypoparathyroidism [8]. However, normal blood calcium levels during pregnancy do not prevent adverse outcomes during pregnancy [9]. The physiological changes of pregnancy, with hemodilution and hypoproteinemia, tend to mask hypercalcemia during pregnancy; It is recommended to measure ionized calcium which is the metabolically active form. The increase

in ionized calcium is the cause of complications [4]. These physiological changes modifications during pregnancy can explain the normal calcium levels throughout the pregnancy in our patient despite the occurrence of neonatal and maternal complications. The increased calcium ionized could explain this maternal complication. Thus, the transient neonatal hypercalcemia diagnosed at two weeks of age could be related to excess calcium that crosses the mother to the fetus via the placenta. This hypothesis seems to be more probable. However, a multiple endocrine neoplasia type 2A (MEN 2A), which would be confirmed by genetic testing for a mutation in the RET proto-oncogene is less probable given the age of the infant. The newborn presented macrosmoia and it seems to be an isolated complication because the classics risk factors of macrosomia such as diabete, obesity, previously delivery of macrosomia or prolonged pregnancy are not presents in our patient. In the literature there is no direct relationships between hypercalcemia and macrosomia. In many case series, surgery, preferably performed before conception or in the second trimester of pregnancy, significantly reduces obstetric and neonatal complications [9] [10]. The medical management, including calcitonin and cinacalcet, are not used during pregnancy due to limited safety data, and the use of biphosphonate therapy must be avoided due to risk of adverse effects on fetal skeletal development [11].

4. Conclusion

Hyperparathyroidism during pregnancy requires early diagnosis and appropriate treatment to reduce obstetric and neonatal complications. The therapeutic approach must be discussed in a multidisciplinary setting. Surgery for parathyroid adenoma reduces complications.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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