Pseudohypoparathyroidism During Pregnancy:

A Rare Disease with Significant Diagnostic, Clinical and Hereditary Consequences for Mother and Neonate

Sara J. Hitt, MS2[1]; Claire McCarthy, MS3[1]; Renee Ricci DO[2]; Bethany Bowling MS3[1]; Anthony B. Royek MD[2]
1. Mercer University School of Medicine. 2. Memorial Health University Medical Center, Department of Obstetrics & Gynecology

Background

- Pseudohypoparathyroidism (PHP) type 1b is a rare, genetically heterogenous condition due to abnormal methylations in the GNAS1 gene [1]. This leads to resistance to parathyroid hormone (PTH).
- Patients may also develop resistance to other hormones such as thyroid-stimulating hormone (TSH), calcitonin, and growth hormone-releasing hormone (GHRH).
- Patients with PHP typically suffer from hypocalcemia and hyperphosphatemia due to the oversecretion of PTH [1].
- During pregnancy, there are significant changes in calcium and active vitamin D homeostasis.
- Patients diagnosed with PHP require careful monitoring and frequent adjustments to pharmacological management due to changes in calcium and vitamin D requirements [2].
- Inadequate serum monitoring and treatment may result in fetal and neonatal hyperparathyroidism as well as an increased risk of neonatal hypoglycemia and respiratory depression.
- Due to the rarity of this disease, there is limited data discussing the management of PHP during pregnancy and birth.

Case Presentation

- A 27-year-old primigravida at 26 weeks EGA was referred to our high-risk OB clinic for maternal management of PHP type 1b and hypothyroidism.
- She was taking calcitriol capsules 0.25 mcg twice a day, vitamin D 1000 units daily, levothyroxine 25 mcg daily, and prenatal vitamins.
- Labs showed a free T4 at 0.53, intact PTH at 51, ionized calcium at 4.9, and phosphorus at 4.6. The patient's endocrinologist monitored calcium, phosphorus, and thyroid function tests frequently during pregnancy.
- At 35 weeks 4 days EGA, she presented to the clinic in preterm labor with painful contractions and vaginal bleeding. She was escorted to the labor and delivery unit for further obstetric management.

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Case Presentation (continued)

- Although the endocrinologist expressed concern over the ability of the uterus to contract effectively, the patient progressed normally in labor and delivered a 2620g female neonate vaginally. Apgar scores were 8/9.
- The neonate was admitted to the NICU for observation and serial assessment of serum calcium and glucose.
- A neonatal hypoparathyroidism gene panel revealed:
- **A sequence variant of the GCM2 gene** - associated with autosomal dominant hyperparathyroidism and autosomal recessive familial hypoparathyroidism
- **A duplication within the GNAS locus** - associated with maternally-inherited autosomal dominant pseudo-hypoparathyroidism type 1a, type 1b and type 1c.
- The patient had an uneventful postpartum course and was discharged home on postpartum day 2.
- The neonate had mild hypocalcemia and high parathyroid hormone 2 days after birth and a pediatric endocrinologist was consulted. After a 4-day NICU admission, the neonate was discharged home.

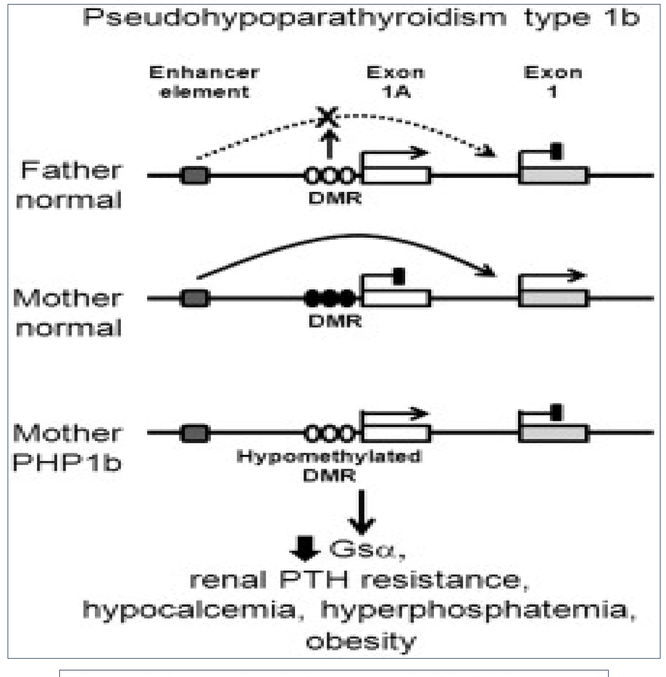

Figure 1. Imprinting defect seen in GNAS1 gene of affected mothers with PHP type 1b. [3]

Conclusion

- This case highlights the importance of multidisciplinary care and collaboration in pregnancies complicated by PHP.
- Due to the nature of this disorder, frequent monitoring and adjustments to medical management are necessary to accommodate the physiological changes and demands during pregnancy.
- The patient in this case was able to have a successful vaginal delivery, uneventful postpartum course, and short NICU admission for her neonate.
- Multidisciplinary management improves outcomes by limiting adverse events, such as maternal and neonatal metabolic derangements.

References

- 1. Linglart, A., Levine, M. A., & Jüppner, H. (2018). Pseudohypoparathyroidism. Endocrinology and metabolism clinics of North America, 47(4), 865–888. https://doi.org/10.1016/j.ecl.2018.07.011
- 2. Marcucci, G., Altieri, P. et al "Hypoparathyroidism Working Group" affiliated to the Italian Society of Endocrinology (S.I.E.) (2021). Hypoparathyroidism and pseudohypoparathyroidism in pregnancy: an Italian retrospective observational study. Orphanet journal of rare diseases, 16(1), 421. https://doi.org/10.1186/s13023-021-02053-3
- 3. Jan de Beur, S. M., & Levine, M. A. (2016). Pseudohypoparathyroidism - an overview | ScienceDirect Topics. https://www.sciencedirect.com/topics/medicine-and-dentistry/pseudohypoparathyroidism