

Parathyroid Tumor Accidentally Discovered During Care of A Lady with Hyperemesis Gravidarum

Medhat M Fadel 1, Mohamed A Mohamed Abouzeid 2, Khine M M Lwin 3

1- Department of Obstetrics and Gynaecology, Ormskirk and Southport District hospital UK

2-Department of internal medicine, Liverpool Royal Hospital, UK

3- Department of Obstetrics and Gynaecology, Manchester Foundation Trust (Wythenshawe Hospital), UK

ABSTRACT

Background: Parathyroid adenoma, a rare but significant endocrine disorder, is often overshadowed by more common conditions during pregnancy, such as hyperemesis gravidarum. Hyperparathyroidism, which primarily results from a solitary parathyroid adenoma in 80-85% of cases, is characterized by the excessive production of parathormone (PTH), leading to hypercalcemia. This disorder is predominantly seen in women aged 50-70 years, and its occurrence in younger populations, particularly during pregnancy is uncommon.

Subject and methods: A 37-year-old multiparous woman, at 13 weeks of gestation, experienced severe vomiting resistant to standard treatment for hyperemesis gravidarum. Hyperemesis gravidarum, a condition marked by severe and persistent nausea and vomiting during pregnancy, typically manifests in the first trimester and can lead to significant maternal and fetal morbidity. When hyperemesis gravidarum is resistant to standard treatment protocols, it necessitates a thorough investigation for atypical etiologies. One such rare but critical differential diagnosis is hyperparathyroidism due to parathyroid adenoma, which can present with elevated calcium levels and refractory vomiting. Diagnosing parathyroid adenoma during pregnancy poses unique challenges. Routine diagnostic procedures for hyperparathyroidism include ultrasound and nuclear imaging techniques such as single-radioisotope scintigraphy with ^{99m}Tc and SPECT imaging, which boast high sensitivity for parathyroid localization. However, the use of ionizing radiation is contraindicated in pregnancy, steering the preference towards non-ionizing imaging modalities like MRI, despite its comparatively lower sensitivity range of 40-85%.

Management: Management of hyperparathyroidism during pregnancy requires a multidisciplinary team (MDT) approach to ensure both maternal and fetal safety. Minimally invasive parathyroidectomy has emerged as the gold standard treatment, especially given the predominance of single adenomas, and has largely supplanted traditional bilateral four-gland exploration. **Conclusion:** Early diagnosis, a multidisciplinary approach, and timely surgical intervention are crucial for optimal outcomes. This case underscored the importance of considering rare endocrine causes in persistent hyperemesis gravidarum and demonstrated the success of minimally invasive surgery in managing this condition effectively.

Keywords: Parathyroid adenoma, Hyperparathyroidism, Pregnancy, Hyperemesis gravidarum, Hypercalcemia, Parathormone (PTH), Minimally invasive parathyroidectomy, Cyclin D1/PRAD1 gene, non-ionizing imaging, Refractory vomiting, Multidisciplinary team

INTRODUCTION

Parathyroid adenoma, a rare endocrine disorder characterized by excessive production of parathormone (PTH) and resultant hypercalcemia, can represent diagnostic challenges, especially during pregnancy. Hyperemesis gravidarum, a common cause of severe vomiting in early pregnancy, typically responds to conventional treatments. However, when symptoms are refractory, it is crucial to explore fewer common etiologies. This case report highlighted a rare instance of parathyroid adenoma masquerading as hyperemesis gravidarum, emphasizing the importance of considering endocrine abnormalities in the differential diagnosis of persistent vomiting in pregnant patients [1,2].

This case report illustrated the importance of considering rare etiologies in the differential diagnosis of hyperemesis gravidarum. It underscores the critical role of MDT in the accurate diagnosis and management of hyperparathyroidism in pregnancy, highlighting that timely surgical intervention can lead to significant

symptomatic relief and favorable outcomes. This case adds to the growing body of literature advocating for a high index of suspicion and comprehensive evaluation in refractory cases of hyperemesis gravidarum to identify underlying endocrine disorders such as parathyroid adenoma [3,4].

CASE REPORT

A 37-year-old multiparous woman, at 13 weeks of gestation, experienced severe vomiting resistant to standard treatment for hyperemesis gravidarum. She had no significant medical, surgical, or obstetric history. Routine investigations revealed elevated calcium levels without an obvious cause.

Further tests showed increased parathormone (PTH) levels, suggesting a parathyroid adenoma. A neck MRI confirmed the diagnosis. The patient underwent successful surgical removal of the adenoma at a specialized center.



Figure (1): CT scan neck showed parathyroid adenoma

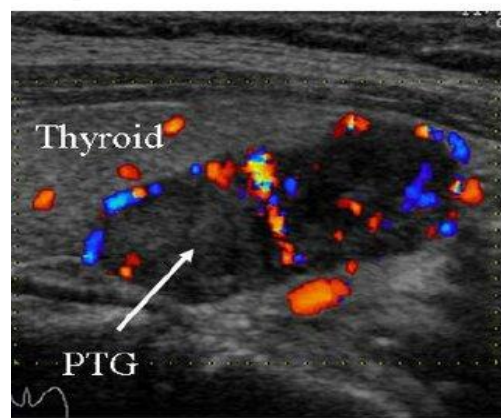
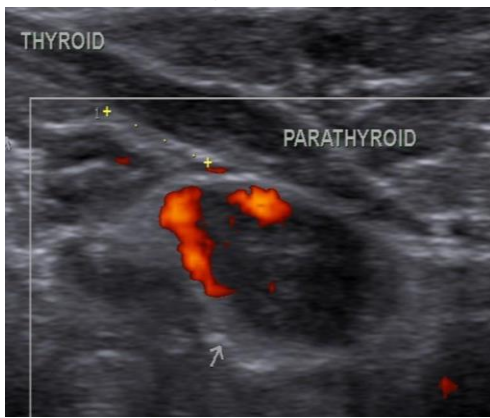


Figure (2,3) U/S scan for the neck region showed enhanced vascularity over the parathyroid gland and associated tumor suggestive for adenoma.

DISCUSSION

Hyperparathyroidism is primarily due to single adenomas (80-85%) but can also be caused by double adenomas (4-5%), hyperplasia (10-12%), and rarely carcinomas (less than 1%). Typically affecting individuals aged 50-70 years. Parathyroid adenomas are more common in women. The etiology is often unclear, but a genetic mutation in the cyclin D1/PRAD1 gene is a common factor. Environmental influences like past radiation therapy and chronic calcium deficiency may also contribute [1, 2, 3]. Genetically, sporadic parathyroid adenomas are frequently associated with mutations in the cyclin D1/PRAD1 gene, which disrupts normal parathyroid function and PTH secretion. Environmental factors, such as previous radiation therapy, and conditions like prolonged calcium deficiency, which stimulate chronic PTH production, are recognized contributors to the development of parathyroid adenomas [4].

Diagnostic tools for hyperparathyroidism included ultrasound (60-80% sensitivity), with single-radioisotope scintigraphy with ^{99m}Tc and SPECT imaging being the gold standard (91-98% sensitivity). Four-dimensional CT and MRI (sensitivities of 75% and 40-85%, respectively)

were also used. During pregnancy, non-ionizing methods like MRI are preferred [4, 7].

Differential diagnoses include:

1. Malignancy-associated hypercalcemia typically presents with higher ion concentrations than benign parathyroid diseases.
2. Familial hypocalciuric hypercalcemia (FHH), up to 20% show elevated PTH levels, distinguished by low urine calcium excretion.
3. Thiazide diuretics and lithium are known to increase calcium levels, identified via medical history.

A multidisciplinary team (MDT) approach is crucial for management. Minimally invasive parathyroidectomy, the gold standard for treating single adenomas, has largely replaced traditional bilateral four-gland exploration. The patient experienced significant symptom improvement post-surgery, with histological examination confirming the diagnosis. No further treatment was required.

Management: The management of parathyroid adenoma in pregnancy began with a thorough initial assessment and accurate diagnosis. Clinically, this involved taking a detailed patient history and conducting a comprehensive physical examination, focusing on symptoms such as

severe vomiting, fatigue, and dehydration. Biochemical tests are crucial, with elevated serum calcium levels indicating hypercalcemia and elevated parathormone (PTH) levels confirming primary hyperparathyroidism in the presence of high calcium [7,8,9]. Imaging studies play a vital role in diagnosing parathyroid adenoma. An ultrasound is often the first non-invasive imaging technique used to detect parathyroid enlargement. During pregnancy, MRI is preferred over other imaging modalities due to its non-ionizing nature, which avoids potential harm to the fetus. MRI helps confirm the presence and precise location of the adenoma [7].

Differential diagnosis is essential to exclude other causes of hypercalcemia, such as malignancy-associated hypercalcemia, familial hypocalciuric hypercalcemia (FHH), and hypercalcemia induced by medications like thiazide diuretics and lithium. This comprehensive approach ensures that the underlying cause of the symptoms is correctly identified [8]. A multidisciplinary team (MDT) approach is critical in managing this condition, involving collaboration among endocrinologists, obstetricians, surgeons, and radiologists. Regular consultations and coordinated planning are necessary to ensure the safety and well-being of both the mother and the fetus [8].

The definitive treatment for parathyroid adenoma is surgical intervention, specifically minimally invasive parathyroidectomy, which is considered the gold standard for treating solitary adenomas. This procedure is preferred over traditional bilateral four-gland exploration due to its reduced operative time and lower complication rates. The timing of the surgery is crucial and is ideally performed in the second trimester to minimize risks to the fetus [6,9].

Preoperative preparation involved stabilizing serum calcium levels through hydration and, if necessary, medications. Adequate maternal and fetal monitoring was essential during this period. Postoperative care focused on monitoring serum calcium levels to prevent hypocalcemia and included histological examination of the excised adenoma to confirm the diagnosis. Regular follow-up is necessary to monitor the health of both mother and fetus [9]. Supportive care is an integral part of managing parathyroid adenoma in pregnancy. This included managing hydration and electrolyte levels through intravenous fluids and electrolyte replacement as needed. Safe antiemetic therapy helped control vomiting, and nutritional support ensured adequate intake and prevented weight loss.

Regular antenatal visits are crucial for monitoring the progress of the pregnancy, with periodic assessments of serum calcium and PTH levels post-surgery. Imaging studies, such as ultrasounds, are used to monitor fetal development and ensure continued well-being [8,9].

Patient education and counseling are vital components of management. Informing the patient about

the nature of the condition, the importance of surgical intervention, and discussing potential risks and benefits are essential. Providing psychological support and counseling helps address any concerns related to the condition and its management [9].

CONCLUSION

Managing parathyroid adenoma during pregnancy requires a delicate balance between addressing the maternal condition and ensuring fetal safety. Early diagnosis, a multidisciplinary approach, and timely surgical intervention are crucial for optimal outcomes. This case underscored the importance of considering rare endocrine causes in persistent hyperemesis gravidarum and demonstrated the success of minimally invasive surgery in managing this condition effectively.

Ethical Approval: This case study has been published after a written informed consent from the patient, all related information and images have been kept strictly confidential and the publication is kept anonymous.

Conflicts of interest: The authors declared that there were no conflicts of interest regarding the publication of this case report.

Funding: The authors received no financial support for the research, authorship, and/or publication of this article.

REFERENCES

1. **Fraser D (2009):** Hyperparathyroidism. *The Lancet*, 374 (9684): 145-158 doi:10.1016/S0140-6736(09)60507-9
2. **Khan A, Hanley A, Rizzoli R, Bollerslev J, Young M, Rejnmark L et al. (2017):** Primary hyperparathyroidism: review and recommendations on evaluation, diagnosis, and management. *Osteoporosis International*, 28 (1): 1-19 doi:10.1007/s00198-016-3716-2
3. **Wells A, Asa L (2014):** Parathyroid adenoma: guidelines for the management of asymptomatic primary hyperparathyroidism: summary statement from the Fourth International Workshop. *Journal of Clinical Endocrinology & Metabolism*, 99 (10): 3561-3569 doi:10.1210/jc.2014-1414
4. **Fitzpatrick A, Bilezikian P (1994):** Hypercalcemia in pregnancy. *Endocrinology and Metabolism Clinics of North America*, 23 (1): 177-186 doi:10.1016/S0889-8529(18)30015-4
5. **Maruani G, Hertig A, Paillard M, Houillier P (2003):** Normocalcemic primary hyperparathyroidism: evidence for a generalized target-tissue resistance to parathyroid hormone. *Journal of Clinical Endocrinology & Metabolism*, 88 (10): 4641-4648 doi:10.1210/jc.2003-030491
6. **Chen H, Sippel S (2011):** Re-operative parathyroidectomy: techniques for a successful operation. *Journal of Surgical Oncology*, 103 (1): 74-79 doi:10.1002/jso.21790
7. **McMullen T, Learoyd D, Williams D, Sidhu S (2015):** Parathyroid adenoma in pregnancy: a rare but important clinical entity. *Journal of Surgical Case Reports*, 2015(3): rjv026 doi:10.1093/jscr/rjv026
8. **Fugazzola L, Caturegli P (2014):** Parathyroid disorders in pregnancy: hyperparathyroidism and hypoparathyroidism. *Best Practice & Research Clinical Endocrinology & Metabolism*, 28 (3): 541-547 doi: 10.1016/j.beem.2014.01.005
9. **Kreidieh N, Ragusa F (2020):** Parathyroid disorders during pregnancy: implications for maternal and fetal outcomes. *Endocrine*, 68 (3): 584-592.