AUCTORES
Globalize your Research

Journal of Obstetrics Gynecology and Reproductive Sciences
Mirna Sanchez Carvallo *

Open Access

Case Report

Follow-up and Clinical Management of a Pregnant Woman with Primary Hyperparathyroidism Associated with Multiple Endocrine Neoplasia Type 1: A Case Report

Mirna Sanchez Carvallo [1]*, Esther Haddas Figueiredo Duarte [2], Isabela Alves Saraiva de Sousa [2], Erika Naliato [3], Leandro Miranda Alves [4], Lenita Zajdenverg [5], Marcos Miranda Oliveira [6], Delmar Muniz Lourenço Junior [7], Alice Helena Dutra Violante [1,2]

[1]Pós-graduação em Endocrinologia, Faculdade de Medicina, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brasil.

[2]Faculdade de Medicina, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brasil.

[3]Ricardo A T Castilho Centro de Estudos, Associação Médica de Teresópolis, Teresópolis, Brasil.

[4]Laboratorio de Endocrinología Experimental - LEEx, Instituto de Ciencias Biomédicas, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brasil

[5]Departamento de Medicina Interna, Serviço de Diabetes da Maternidade - Escola, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brasil.

[6]Maternidade Escola da Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brasil.

[7]Hospital das Clínicas FMUSP, Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brasil.

***Corresponding Author:** Mirna Sanchez Carvallo, Pós-graduação em Endocrinologia, Faculdade de Medicina, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brasil.

Received date: July 04, 2025; **Accepted date:** July 25, 2025; **Published date:** July 31, 2025.

Citation: Mirna S. Carvallo, Figueiredo Duarte EH, Isabela Alves Saraiva de Sousa, Erika Naliato, Alice Helena Dutra Violante, Leandro Miranda Alves, Lenita Zajdenverg, Marcus Miranda Oliveira and Delmar Muniz Lourenço Jr., (2025), Follow-up and Clinical Management of a Pregnant Woman with Primary Hyperparathyroidism Associated with Multiple Endocrine Neoplasia Type 1: A Case Report, *J. Obstetrics Gynecology and Reproductive Sciences*, 9(5) **DOI:10.31579/2578-8965/275**

Abstract:

Introduction: Studies on clinical implications and management of endocrine tumors in pregnant women with Multiple Endocrine Neoplasia Type 1 (MEN1) are limited to case reports or small series, which challenges individualized treatment decision making. Potential risks of maternal and fetal complications related to MEN1 neoplasms, such as primary hyperparathyroidism (PHPT) and prolactinoma, are primarily known from studies on sporadically occurring tumors.

Case Description: A 38-year-old woman with MEN1 developed mild and sustained hypercalcemia (serum calcium: 10.36 ± 0.32, 9.9-10.8 mg/dL) due to PHPT, throughout her pregnancy, leading to careful periodic laboratory surveillance without specific therapeutic intervention. Progressive intrauterine fetal growth restriction during the third trimester resulted in a cesarean section birth at term (at 38 weeks and 4 days) of a low birth weight for gestational age newborn (< 3rd percentile: 2115 grams).

Conclusions: This case highlights the need for monitoring the progression of intrauterine growth in pregnant women with PHPT associated with MEN1. Since there are no established guidelines for the clinical or surgical management of PHPT in pregnant women with MEN1, treatment decisions should be individualized and made by a specialized multidisciplinary team, based primarily on experience, albeit limited, from sporadic cases of PHPT.

Keywords: multiple endocrine neoplasia type 1; primary hyperparathyroidism; pregnancy; hypercalcemia; fetal growth restriction

Introduction

Multiple Endocrine Neoplasia Type 1 (MEN1) is a rare genetic syndrome caused by germline mutations in the MEN1 tumor suppressor gene (chromosome 11q13), which encodes the MENIN nuclear protein, an ubiquitin ligase that regulates transcription, genome stability, and cellular division and proliferation. Germline mutations in the MEN1 gene — deletions, insertions, missense, or nonsense mutations — inactivate this protein, leading to loss of its tumor-suppressing function, and thus predisposing individuals to the development of endocrine tumors that primarily affect pituitary, gastrointestinal tract, and parathyroid glands [1-3].

The estimated prevalence of the syndrome is 3-20 cases per 100,000 individuals, and it affects predominantly women [4]. More than 80% of individuals with a MEN1 germline mutation will present clinical manifestations at the fifth decade of life [5], marking its high penetrance, which is virtually complete at older ages, particularly characterized by primary hyperparathyroidism (PHPT) and non-functioning pancreatic neuroendocrine tumors (NETs). Therefore, these tumors are the most prevalent in MEN1, followed by gastrinoma and prolactinoma. Other pituitary tumors, such as growth hormone-secreting, ACTH-secreting, and non-functioning tumors, as well as other pancreatic NETs, such as insulinomas and glucagonomas, occur less frequently in MEN1. In addition, other endocrine tumors, such as thymic, pulmonary, and gastric NETs, as well as adrenal cortical adenomas, dermal tumors (lipomas, angiofibromas, collagenomas), and other non-endocrine tumors like meningiomas, leiomyomas, and ependymomas, may also develop with variable prevalence [5-7].

Clinical diagnosis of MEN1 is established by the presence of tumors affecting at least two of the three main endocrine glands associated with MEN1: parathyroid, pituitary, and pancreatic/duodenal endocrine tissue. The diagnosis of familial MEN1 can be established when a first-degree relative of a confirmed MEN1 patient also presents at least one endocrine tumor affecting one of these tissues/glands. Molecular diagnosis is made by identifying a MEN1 germline mutation in an individual, regardless of phenotype [4-8].

The scarcity of studies and specific guidelines for the management of pregnant women with MEN1 significantly challenges follow-up and treatment. The rarity of MEN1, combined with the multiplicity of tumor manifestations, requires individualized and multidisciplinary approach.

Hogg et al. identified an increased risk of maternal and fetal complications in 26 women with MEN1 throughout 96 pregnancies, as they were more prone to hypertensive disorders, gestational diabetes, premature birth, and low birth weight offspring [9].

The risk of complications during pregnancy varies according to the clinical manifestations of the syndrome. The presence of PHPT has been associated with higher risk of hypertensive disorders, hyperemesis gravidarum, nephrolithiasis, and pancreatitis, as well as intrauterine growth restriction and neonatal hypocalcemia [10]. Pregnant women with prolactinoma are at a higher risk of pituitary adenoma enlargement and, consequently, pituitary apoplexy and visual disturbances [11]. Given this complexity, pre- and perinatal follow-up of pregnant women with MEN1 by an experienced and multidisciplinary team is crucial to ensure the well-being of both mother and child, as more than one endocrine tumor with potential risks to both may synchronously occur.

We present the case of a pregnant woman with MEN1, highlighting the endocrine manifestations of the syndrome during pregnancy and the strategies employed to optimize maternal and fetal outcomes.

Case Presentation

At 23 years of age, following an endocrine investigation due to menstrual irregularity, a female patient was diagnosed with a microprolactinoma and started on dopamine agonist treatment (cabergoline), exhibiting an excellent response, with normalization of serum prolactin levels and involution of the tumor lesion at pituitary magnetic resonance imaging (MRI).

Four years later, the patient and her brother were referred to the Endocrinology Outpatient Clinic at the Clementino Fraga Filho University Hospital (HUCFF) for genetic counseling, since their mother had been clinically diagnosed with MEN1 (Table 1).

Cases	Age at clinical / molecular diagnosis (years)	Morbidities
Proband (mother)	46 / 52	Prolactinoma PHPT Adrenocortical tumor (NF) Insulinoma
Brother	34 / 38	PHPT Metastatic thymic NET
Pregnant (present case)	23 / 28	Prolactinoma PHPT Bronchial NET Adrenocortical tumor (NF)

Table 1: Clinical features of a pregnant woman with MEN1 and her affected family members harboring the nonsense germline pathogenic variant c.1177C>T (p.Q393).

PHPT: primary hyperparathyroidism; **NF:** non-functioning

Molecular analysis of these three family members, performed at the Faculty of Medicine of the University of São Paulo (FMUSP), revealed a pathogenic germline variant, in heterozygosity, nonsense (c.1177C>T; p.Q393) in exon 8 of the MEN1 gene (Figure 1).

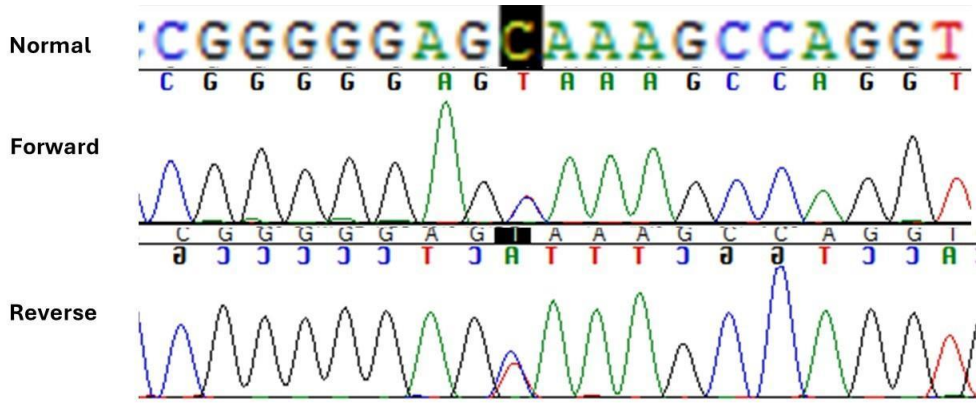

Figure 1: A pathogenic variant was initially found in the proband and her two siblings, including her pregnant daughter with primary hyperparathyroidism and prolactinoma. The normal MEN1 reference sequence, as well as the forward and reverse sequences amplified from the proband (mother), are illustrated, revealing a change from cytosine to thymine at position 1177 of the complementary DNA (c.1177C>T) located in exon 8 of the MEN1 gene, resulting in a stop codon corresponding to codon 393 of the MENIN protein, which encodes the amino acid glutamine, generating a truncated protein with 392 amino acids.

Due to the diagnosis of familial MEN1, active laboratory surveillance of calcium, phosphate, and parathyroid hormone levels was initiated. Over the first 11 years of follow-up, her serum calcium levels remained at the upper normal limit with concomitant inappropriately normal or non-suppressible PTH levels - characterizing mild primary hyperparathyroidism (PHPT). The patient subsequently developed sustained mild hypercalcemia and elevated PTH levels (Table 2). Bone densitometry was performed, showing a 4% decrease in femoral neck bone density over a 7-year period.

Year	Calcium (mg/dL)	Phosphorus (mg/dL)	PTH (pg/mL)
2007	9.7	3.6	47.7
2008	9.6	3.5	43.3
2009	10.1	3.6	51.4
2010	9.6	3.3	-
2011	-	-	-
2012	-	-	-
2013	10.1	3.8	66.4
2014	10.1	3.6	50.3
2015	9.3	2.7	36.0
2016	9.9	3.4	62.3
2017	10.0	3.0	76.3
2018	10.5	3.5	94.4

Table 2: Calcium, phosphorus and PTH levels (2007-2018)

Reference values: Calcium = 8.5 -10.2 mg/dL; Phosphorus = 2.5 - 4.5 mg/dL; PTH = 12 - 65pg/mL

Given these persistent changes, parathyroid scintigraphy was performed and detected persistent 3h-uptake of sestamibi by the lower right cervical region, suggesting the presence of a parathyroid adenoma. The patient was referred to a parathyroidectomy. However, surgery was not performed, since the patient returned to the outpatient clinic reporting an ongoing pregnancy. At that moment, dopamine agonist treatment was discontinued and the 38-year-old patient was subsequently referred to the Maternity School of the Federal University of Rio de Janeiro (UFRJ) for prenatal follow-up by a multidisciplinary team at 7 weeks and 3 days of gestation. During the first consultation, she was counseled about the possibility of parathyroidectomy during the second trimester of pregnancy.

In the first trimester of pregnancy, daily treatment with levothyroxine 88 mcg was initiated following the diagnosis of subclinical hypothyroidism [thyroid-stimulating hormone (TSH) = 5.29 mU/L, (reference range: 0.1 – 2.5 mU/L); free T4 = 0.9 ng/dL (reference range: 0.7-1.9 ng/dL); negative anti-thyroid peroxidase (TPO) antibody]. Daily vitamin D supplementation of 2000 IU was initiated, with dose adjustments throughout pregnancy based on serum levels of 25-OH vitamin D (Table 3). Starting at the 12th week of pregnancy, acetylsalicylic acid (ASA) was initiated at a dose of 100 mg/day for preeclampsia prophylaxis.

She progressed without complications associated with PHPT, maintaining mild hypercalcemia without hypercalciuria or nephrolithiasis (Table 3). Blood pressure remained normal throughout the prenatal follow-up.

Gestational age	7W3D	11W	13W	14W6D	17W5D	21W4D	26W6D	30W2D	36W	37W6D
Calcium (mg/dL)	10.6	10.6	10.8	10.5	10.1	10.2	9.9	10.0	10.6	-
Ionized calcium (mg/dL)	-	5.3	5.5	-	5.3	5.4	5.6	5.65	5.97	-
Phosphorus (mg/dL)	3.1	2.9	3.5	-	3.6	2.7	3.9	3.6	3.2	-
PTH (pg/mL)	68	72	58	79	-	61	61	57	65	-
25-OH vitamin D (ng/mL)	16.3	21.2	21.2	16.5	-	22.1	14.5	19.2	19.5	-
Glucose (mg/dL)	94	82.6		83	-	-	76	77.8	-	-
OGTT (mg/dL)	-	-	-	-	-	-	1h: 124 2h:123	-	-	-
24 h-urinary calcium (mg/24h)	173.5	-	-	-	248.6	-	-	-	-	-
Proteinuria (mg/24h)	-	-	-	-	-	-	-	-	-	300
Albumin (g/dL)	4.9	4.2	4.2	4.0	3.9	3.8	3.3	3.4	3.3	-
TSH (mU/L)	5.29	-	-	0.918	0.918	1.87	0.896	0.991	1.26	-
TPO (U/mL)	-	-	-	19	-	-	-	-	-	-

Table 3: Laboratory exams assessed during pregnancy.

***W:** weeks; **D:** Days*

Reference values: Calcium = 8.5 -10.2 mg/dL; Ionized calcium = 4.0 - 5.0 mg/dL; Phosphorus = 2.5 - 4.5 mg/dL; PTH = 12 - 65pg/mL; 25-OH vitamin D = 30 - 60 ng/mL; Fasting glucose= 92 mg/dL; OGTT: 1h < 180 mg/dL, 2h < 153 mg/dL; 24h-urinary calcium < 300 mg/24h; Proteinuria < 300 mg/24h; Albumin = 3.5 - 4.7 g/dL; TSH 1st trimester = 0.1 - 2.5, 2nd trimester = 0.2 - 3.0; 3rd trimester = 0.3 - 3.0 mU/L; TPO < 34 U/mL.

A fetal ultrasonography (USG) performed at 32 weeks and 3 days of gestation showed fetal weight of 1,652 g (10.6th percentile). Five weeks later, fetal weight was 2,387 g (4.9th percentile) and a cardiotocography showed a reactive pattern, consistent with good fetal vitality.

At 38 weeks and 2 days of gestation, the patient was admitted to the maternity ward for labor induction. After 2.5 days of induction, despite good progression of uterine contractions and adequate cervical effacement, there was a halt in fetal descent and elective cesarean section was indicated. The female neonate was small for gestational age (weight= 2115 g, below the 3rd percentile) with Apgar scores of 8 and 9 at the first and fifth minutes, respectively. The baby was in good clinical condition at birth without neonatal hypocalcemia. During the puerperal period, no signs of post-partum hyperparathyroid crisis were observed. Breastfeeding occurred on demand and hospital discharge occurred 48 hours after birth.

Clinical conditions frequently associated with intrauterine growth restriction, such as gestational hypertension, placental insertion defects, smoking, malnutrition, congenital infectious diseases, such as toxoplasmosis, syphilis, cytomegalovirus, rubella, HIV, hepatitis, genetic dysmorphisms or inborn metabolic errors were excluded.

Two years after delivery, the patient returned to the endocrinology outpatient clinic with laboratory tests revealing mild PHPT (Calcium = 10.8 mg/dL; PTH = 86 pg/mL). Despite remaining out of dopamine agonist treatment since the detection of pregnancy, normal prolactin levels and a pituitary magnetic resonance imaging revealing a stable pituitary adenoma measuring 0.6 cm x 0.4 cm were obtained. During preoperative evaluation for parathyroidectomy, she was diagnosed with a neuroendocrine bronchial tumor greater than 2 cm and treated with octreotide LAR and parathyroidectomy was once again suspended. Four years after her pregnancy, a computed tomography scan revealed the presence of a non-functioning adrenal adenoma measuring 1.6 cm.

Presently, although parathyroidectomy was not performed due to the significant morbidity of the other manifestations, the patient remains asymptomatic without bone or renal complications.

Discussion

Women with MEN1 germline mutations are at high risk of developing various types of tumors, which in their sporadic form could interfere with both fertility and pregnancy. However, studies on pregnant women with MEN1 are limited, consisting mostly of case reports and two large retrospective Australian studies [9,12-17].

Turner et al. highlighted the crucial role of family history on MEN1 detection and suggested that even individuals without evident clinical manifestations must be considered for diagnostic scrutinization of MEN1 when specific endocrine tumors are identified in another family member. The goal of follow-up is to detect early manifestations of the syndrome and implement appropriate preventive and therapeutic measures [8].

In a 10-year retrospective study, Lourenço Jr et al. demonstrated the impact of genetic testing family members at risk for MEN1 on appropriate clinical management of the syndrome, observing that asymptomatic young individuals carrying the MEN1 mutation benefited from early detection of endocrine tumors [18]. Early diagnosis of tumors is possible through periodic hormonal and radiological screening suggested by guidelines for carriers of the MEN1 germline mutation [4-7].

Tumors that manifest during pregnancy have been associated with complications, such as miscarriage, prematurity, and increase both maternal and fetal mortality [9]. Therefore, counseling aimed at planning the best timing for conception and implementation of appropriate preventive and therapeutic measures is essential for women with MEN1 who wish to conceive.

Studies on the management of PHPT and prolactinoma in MEN1 during pregnancy are scarce [4-7,9,12-17,19] and no clinical guideline has addressed this subject.

In women with MEN1, the incidence of pituitary tumors is high (15% to 50%) with prolactinoma being the most common (approximately 65%) and not rarely the first manifestation of the syndrome [4-8]. Symptoms of hyperprolactinemia in MEN1 do not differ from those observed in sporadic prolactinomas [20]. During pregnancy, increased estrogen levels can stimulate the growth of prolactinomas in 2-3% of micro- and 31% of previously untreated macroprolactinomas [21,22]. During her pregnancy follow-up, our patient was monitored for tumoral growth with no need for dopaminergic agonist therapy.

PHPT is the most frequent endocrine manifestation in MEN1, with a prevalence of 90%. Symptoms include hypercalcemia, nephrolithiasis, polydipsia, polyuria, constipation, osteoporosis, fractures, and impaired quality of life [4-8,23-25]. Parathyroidectomy is the cornerstone of PHPT treatment and generally curative, leading to normalization of calcium levels and resolution of symptoms in sporadic forms. However, in cases with multiglandular disease, such as in MEN1, recurrence and persistence rates are high, even after more extensive surgeries [4-8,23]. During pregnancy, calcium homeostasis changes, resulting in relative fetal hypercalcemia. Maternal serum calcium increases due to a higher production of active vitamin D, increased intestinal calcium absorption, and placental parathyroid hormone-related peptide released in response to estradiol, placental lactogen, and prolactin [26,27]. PHPT may result in maternal hypertensive disorders, hyperemesis gravidarum, nephrolithiasis, pancreatitis, and osteoporosis, fetal death, intrauterine growth restriction and neonatal hypocalcemia [10,14].

Mistry et al. reported the case of a 31-year-old primigravida with MEN1 (macroprolactinoma, PHPT, pancreatic gastrinoma, non-functioning adrenal adenoma, and secondary hypothyroidism). During pregnancy, she developed hypercalcemia, requiring an early cesarean section at 35 weeks due to intrauterine growth restriction (IUGR). The fetus had adequate Apgar score, but developed hypocalcemia, requiring intravenous calcium replacement with good recovery and hospital discharge [12].

McCarthy et al. described three pregnant women with PHPT who underwent surgery in the second trimester, including a 20-year-old patient with MEN1, who had an uneventful pregnancy and delivery [19].

Hogg et al. studied 26 pregnant women with MEN1; 30% with PHPT and peak serum calcium levels observed during the second trimester. They also identified high rates of gestational diabetes mellitus (56%), hypertensive disorders (25.9%) and low birth weight (30.1%) [9].

During pregnancy, 25-OH vitamin D levels tend to decrease due to its role in fetal development, increasing the risk of complications such as preeclampsia, gestational diabetes, prematurity, IUGR, and low birth weight [28,29]. The establishment of target levels of 25-OH vitamin D above 40 ng/mL has been suggested for pregnancy [30]. Daily supplementation of 2000 IU of 25-OH vitamin D was prescribed to our patient, resulting in a peak level of 22.1 ng/mL, at 21 weeks and 4 days of gestation. Low adherence to 25-OH vitamin supplementation might explain the suboptimal levels obtained during this pregnancy follow-up, since by that time the referred medication was not provided by the Brazilian public health system [31].

Early recognition and strict monitoring of PHPT during pregnancy are essential, and management depends on the severity of symptoms, maternal complications, and potential risks to fetal development. Therapeutic options may include hydration, discontinuation of thiazide diuretics, and supplementation of calcium and vitamin D to prevent bone demineralization. Bisphosphonates and denosumab cross the placental barrier, are associated with adverse fetal skeletal effects, and should be avoided [10]. Calcitonin and calcimimetics have been used to control moderate and severe hypercalcemia during pregnancy, despite uncertain evidence on maternal and fetal repercussion, requiring strict monitoring due to potential side effects. Calcitonin reduces calcemia, while cinacalcet decreases both PTH and calcium. [10,32].

During pregnancy, parathyroidectomy is generally considered as a treatment option for PHPT with moderate to severe hypercalcemia (calcium >12 mg/dL) and is performed in the second trimester, when maternal and fetal risk of untreated hyperparathyroidism outweighs the risks of a surgery [10,32].

Based on data from a tertiary center with expertise on endocrine surgery, DiMarco et al. studied a cohort of 17 pregnant women with PHPT in which 15 were submitted to a parathyroidectomy and two did not undergo surgery. The parathyroidectomy subgroup had no cases of fetal distress or miscarriage. Deliveries occurred without complications, except for one membrane rupture at 39 weeks of gestation that resulted in a healthy cesarean section-delivered baby. The two patients who did not undergo surgery, on the other hand, experienced perinatal complications: one developed preeclampsia and delivered an IUGR baby, while the other progressed to a miscarriage [33].

Thompson et al. pointed that neonates of mothers with MEN1 had a higher prevalence of IUGR (MEN1: 28.9% vs. No MEN1: 6.7%). In addition, postnatal mortality was higher in offsprings of MEN1 (HR 4.6; $p = 0.046$ at 6 months of age). However, increased mortality and IUGR rates could not be solely explained by neonatal or maternal hypercalcemia [16].

In the present case report, progressive IUGR started at the 32nd week of gestation, with fetal weight decreasing from the 10.6th to the 4.9th, at week 36, and dropping below the 3rd percentile, at birth. Besides PHPT with sustained maternal hypercalcemia and no spikes, no other maternal condition could be related to the severity of IUGR. The subclinical hypothyroidism diagnosed at the 7th week of pregnancy was promptly treated and remained well-controlled throughout the pregnancy, minimizing its potential impact on the development of IUGR.

Limitations

This case report has some limitations. First, being limited to a single patient, the report inherently limits the generalizability of the findings. While the patient's favorable maternal and neonatal outcomes are encouraging, these results may not be extrapolated to all women with MEN1, especially those presenting with more severe or multisystemic manifestations. Second, the absence of postnatal neurodevelopmental follow-up to assess the impact of IUGR potentially associated with sustained maternal hypercalcemia. Third, the lack of consensus on when to surgically manage PHPT during pregnancy, particularly in cases of mild hypercalcemia, further complicates clinical decisions. Future studies, including prospective registries and comparative cohorts, are essential to guide management and establish standardized care protocols for pregnant women with MEN1.

Conclusions

Pregnant women with MEN1 are prone to developing numerous maternal-fetal complications. Those with PHPT require proper control of calcium, PTH, and vitamin D to reduce the risk of peri- and prenatal complications. More studies on the association between IUGR and MEN1 are necessary to assess the potential impact of MEN1 on fetal growth, including the subset of patients with PHPT and mild hypercalcemia. Significant IUGR development could be used as an additional indication for surgical treatment in the second trimester of pregnancy. This case highlights the importance of extending knowledge regarding the clinical impact of endocrine tumors in pregnant women with MEN1. Due to the rarity of the disease, there is no consensus on the optimal management of these cases. Consequently, definition of management strategies should be individualized, based on the data originated from the treatment of corresponding sporadic endocrine tumors and involve a specialized multidisciplinary team.

Author contributions.

Conception and Design: M.S.C. and A.H.D.V

Data Collection: M.S.C., E.H.F.D. and I.A.S.S. were responsible to data collection

Drafting and Revising the Manuscript: M.S.C., E.H.F.D., I.A.S.S. and D.M.L.J were responsible for drafting the Manuscript. A.H.D.V., L.Z., L.M.A., D.M.L.J, M.M.O and E.N. were responsible to revise the manuscript.

D.M.L.J was responsible for the molecular sequencing.

Supervision: A.H.D.V. and D.M.L.J. were responsible to supervise.

Acknowledgements: The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. Lemos, M. C., & Thakker, R. V. (2008). Multiple endocrine neoplasia type 1 (MEN1): Analysis of 1336 mutations reported in the first decade following identification of the gene. Human Mutation, 29(1), 22–32.
2. Concolino, P., Costella, A., & Capoluongo, E. (2016). Multiple endocrine neoplasia type 1 (MEN1): An update of 208 new germline variants reported in the last nine years. *Cancer Genetics*, 209(1–2), 36–41.
3. Carvalho, R. A., Urtremari, B., Jorge, A. A. L., et al. (2018). Germline mutation landscape of multiple endocrine neoplasia type 1 using full gene next-generation sequencing. *European Journal of Endocrinology*, 179(6), 391–407.
4. Brandi, M. L., Agarwal, S. K., Perrier, N. D., Lines, K. E., Valk, G. D., et al. (2021). Multiple endocrine neoplasia type 1: Latest insights. Endocrine Reviews, 42(2), 133–170.
5. Thakker, R. V., Newey, P. J., Walls, G. V., et al. (2012). Clinical practice guidelines for multiple endocrine neoplasia type 1 (MEN1). The *Journal of Clinical Endocrinology & Metabolism*, 97(9), 2990–3011.
6. Al-Salameh, A., Cadiot, G., Calender, A., Goudet, P., & Chanson, P. (2021). Clinical aspects of multiple endocrine neoplasia type 1. *Nature Reviews Endocrinology*, 17(4), 207–224.
7. Pieterman, C. R. C., & Valk, G. D. (2022). Update on the clinical management of multiple endocrine neoplasia type 1. Clinical Endocrinology, 97(4), 409–423.
8. Turner, J. J., Christie, P. T., Pearce, S. H., Turnpenny, P. D., & Thakker, R. V. (2010). Diagnostic challenges due to phenocopies: Lessons from multiple endocrine neoplasia type 1 (MEN1). *Human Mutation*, 31(1), E1089–E1101.
9. Hogg, P., Thompson, M., & Burgess, J. (2020). The clinical expression and impact of multiple endocrine neoplasia 1 during pregnancy. *Clinical Endocrinology*, 93(4), 429–438.
10. Ali, D. S., Dandurand, K., & Khan, A. A. (2021). Primary hyperparathyroidism in pregnancy: Literature review of the diagnosis and management. *Journal of Clinical Medicine*, 10(13), 2956.
11. Grand'Maison, S., Weber, F., Bédard, M. J., Mahone, M., & Godbout, A. (2015). Pituitary apoplexy in pregnancy: A case series and literature review. *Obstetric Medicine*, 8(4), 177–183.
12. Mistry, M., Gupta, M., & Kaler, M. (2014). Pregnancy in multiple endocrine neoplasia type 1 equals multiple complications. *Obstetric Medicine*, 7(3), 123–125.
13. Daglar, H. K., Kirbas, A., Biberoglu, E., Laleli, B., & Danisman, N. (2016). Management of a multiple endocrine neoplasia type 1 during pregnancy: A case report and review of the literature. *Journal of Experimental Therapeutics and Oncology*, 11(3), 217–220.
14. Guo, J., Gu, N., Wang, W., Yuan, G., & Zhang, J. (2021). Delayed diagnosis of multiple endocrine neoplasia type 1 during pregnancy: A case report. QJM, 114(5), 321–323.
15. Thompson, M., & Burgess, J. (2019). No evidence of adverse fertility and pregnancy outcomes in patients with unrecognized and untreated multiple endocrine neoplasia type 1. *Clinical Endocrinology*, 90(2), 312–319.
16. Thompson, M., Hogg, P., De Paoli, A., & Burgess, J. (2020). Parental multiple endocrine neoplasia type 1 (MEN1) is associated with increased offspring childhood mortality. The *Journal of Clinical Endocrinology & Metabolism*, 105(4), e1084–e1091.
17. Li, J., Xu, D., & Liu, X. (2022). Management of a multiple endocrine neoplasia type 1 during pregnancy: A case with primary hypertension. *Gynecological Endocrinology*, 38(1), 94–96.
18. Lourenço, D. M., Jr., Toledo, R. A., Coutinho, F. L., et al. (2007). The impact of clinical and genetic screenings on the management of the multiple endocrine neoplasia type 1. Clinics, 62(4), 465–476.
19. McCarthy, A., Howarth, S., Khoo, S., et al. (2019). Management of primary hyperparathyroidism in pregnancy: A case series. *Endocrinology, Diabetes & Metabolism Case Reports*, 19-0039.
20. Pieterman, C. R. C., van Leeuwaarde, R. S., van den Broek, M. F. M., et al. (2021). Multiple endocrine neoplasia type 1. In K. R. Feingold, S. F. Ahmed, B. Anawalt, et al. (Eds.), Endotext. MDText.com, Inc.
21. Christin-Maître, S., Delemer, B., Touraine, P., & Young, J. (2007). Prolactinoma and estrogens: Pregnancy, contraception and hormonal replacement therapy. *Annales d'Endocrinologie,* 68(2–3), 106–112.
22. Melmed, S., Casanueva, F. F., Hoffman, A. R., et al. (2011). Diagnosis and treatment of hyperprolactinemia: An Endocrine

Society clinical practice guideline. The *Journal of Clinical Endocrinology & Metabolism*, 96(2), 273–288.

23. Giusti, F., Cianferotti, L., Boaretto, F., et al. (2017). Multiple endocrine neoplasia syndrome type 1: Institution, management, and data analysis of a nationwide multicenter patient database. Endocrine, 58(2), 349–359.
24. Lourenço, D. M., Jr., Coutinho, F. L., Toledo, R. A., Montenegro, F. L., Correia-Deur, J. E., et al. (2010). Early-onset, progressive, frequent, extensive, and severe bone mineral and renal complications in multiple endocrine neoplasia type 1-associated primary hyperparathyroidism. *Journal of Bone and Mineral Research*, 25(11), 2382–2391.
25. Brescia, M. D. G., Rodrigues, K. C., d'Alessandro, A. F., et al. (2022). Impact of parathyroidectomy on quality of life in multiple endocrine neoplasia type 1. Endocrine Connections, 11(6), e220021.
26. Rey, E., Jacob, C. E., Koolian, M., & Morin, F. (2016). Hypercalcemia in pregnancy – A multifaceted challenge: Case reports and literature review. *Clinical Case Reports*, 4(10), 1001–1008.
27. Hu, Y., Cui, M., Sun, Z., et al. (2017). Clinical presentation, management, and outcomes of primary hyperparathyroidism during pregnancy. *International Journal of Endocrinology*, 2017, 3947423.
28. Khalessi, N., Kalani, M., Araghi, M., & Farahani, Z. (2015). The relationship between maternal vitamin D deficiency and low birth weight neonates. *Journal of Family and Reproductive Health*, 9(3), 113–117
29. Dragomir, R. E., Toader, O. D., Gheoca Mutu, D. E., & Stănculescu, R. V. (2024). The key role of vitamin D in female reproductive health: A narrative review. *Cureus*, 16(7), e65560.
30. Jones, G., Strugnell, S. A., & DeLuca, H. F. (1998). Current understanding of the molecular actions of vitamin D. Physiological Reviews, 78(4), 1193–1231.
31. Câmara dos Deputados. (2021). Projeto de Lei nº 3759 de 2021.
32. Horjus, C., Groot, I., Telting, D., et al. (2009). Cinacalcet for hyperparathyroidism in pregnancy and puerperium. *Journal of Pediatric Endocrinology and Metabolism*, 22(8), 741–749.
33. DiMarco, A. N., Meeran, K., Christakis, I., et al. (2019). Seventeen cases of primary hyperparathyroidism in pregnancy: A call for management guidelines. *Journal of the Endocrine Society*, 3(5), 1009–1021.

DOI:10.31579/2578-8965/275