

Concurrent Hyperreactio Luteinalis and Selective Fetal Growth Restriction in a Monochorionic Twin Pregnancy: A Case Report

Concomitância de *Hyperreactio Luteinalis* e Restrição Seletiva de Crescimento Fetal em Gravidez Gemelar Monocoriônica: Relato de Um Caso

Joana Gomes Augusto¹, Maria Fedchenko¹, Joana Torres Silva¹, Sandra Batista¹, Carla Duarte¹

Department of Obstetrics and Gynecology, Gaia/Espinho Local Health Unit, Portugal

Abstract

Hyperreactio luteinalis (HL) is a rare benign ovarian condition of pregnancy characterized by progressive ovarian enlargement and hyperandrogenism, often associated with hypertensive disorders and fetal growth restriction. We report a spontaneous monochorionic diamniotic twin pregnancy complicated by selective fetal growth restriction (sFGR) diagnosed at 18 weeks and concurrent HL. The sFGR progressed from type I to type II with early signs of twin-to-twin transfusion syndrome, prompting delivery at 27 weeks. This rare constellation highlights the importance of clinical suspicion for HL in the presence of adnexal masses in pregnancy and warrants further research on its prognostic implications in monochorionic pregnancies.

Keywords: Adnexal diseases; Fetal growth retardation; Fetofetal transfusion; Luteinizing hormone; Pregnancy.

Resumo

A *hyperreactio luteinalis* (HL) é uma condição ovárica benigna e rara da gravidez, caracterizada por aumento ovárico progressivo e hiperandrogenismo, frequentemente associada a perturbações hipertensivas e restrição do crescimento fetal. Relatamos um caso de gestação gemelar monocoriônica biamniótica espontânea complicada por restrição seletiva do crescimento fetal (sRCF) diagnosticada às 18 semanas e HL concomitante. A sRCF progrediu de tipo I para tipo II com sinais precoces de síndrome de transfusão feto-fetal, motivando o parto às 27 semanas. Esta constelação clínica incomum salienta a importância da suspeição de HL perante a identificação de massas anexiais na gravidez e justifica investigação futura sobre as suas implicações prognósticas em gravidezes monocoriônicas.

Palavras-chave: Doenças dos anexos; Restrição de crescimento fetal; Transfusão feto-fetal; Hormona luteinizante; Gravidez.

INTRODUCTION

Monochorionic twin pregnancies pose significant challenges in obstetric care due to the presence of a shared placenta and intertwin vascular anastomo-

ses. These unique anatomical features predispose to a spectrum of complications that are exclusive to monochorionicity. Among the most challenging complications in this setting is selective fetal growth restriction (sFGR), a major contributor to perinatal morbidity and mortality, with an incidence ranging from 10% to 26% of monochorionic twin gestations¹. When sFGR presents early – before 24 weeks' gestation – it is

1. Department of Obstetrics and Gynecology, Gaia/Espinho Local Health Unit, Portugal.

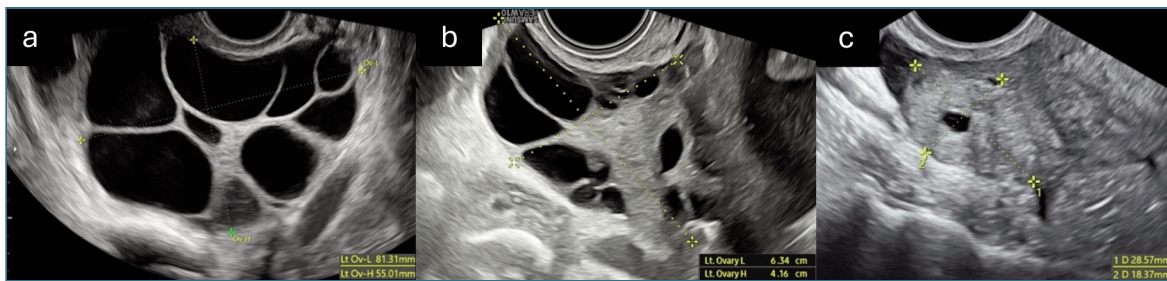


FIGURE 1. Ultrasound images of the left ovary at 12 weeks and 6 days of gestation (a), 23 weeks and 4 days of gestation (b), and 4 weeks postpartum (c). Ov-H, ovary height; Ov-L, ovary width.

associated with a markedly increased risk of superimposed twin-to-twin transfusion syndrome (TTTS), intrauterine fetal demise, severe neonatal morbidity, and long-term neurodevelopmental impairment^{2,3}.

Hyperreactio luteinalis (HL) is an uncommon, benign ovarian condition characterized by bilateral, multicystic ovarian enlargement during pregnancy⁴. Although HL usually follows a self-limiting course with postpartum resolution, it has been associated with significant maternal and fetal complications, correlated with a high beta human chorionic gonadotropin (β -hCG) level, including gestational hypertension, pre-eclampsia, and fetal growth restriction⁵.

Herein, we present a rare and complex case of a spontaneous monochorionic diamniotic twin pregnancy complicated by early-onset sFGR and concurrent maternal hyperreactio luteinalis. We aim to discuss the diagnostic and management challenges posed by this dual pathology and review the implications for maternal and fetal outcomes.

CLINICAL CASE

A 34-year-old primigravida with a spontaneous monochorionic diamniotic twin pregnancy was referred for routine first-trimester ultrasound evaluation at 12 weeks and 6 days of gestation. Fetal anatomical assessment demonstrated no structural anomalies, with concordant crown-rump lengths between the twins. However, sonographic examination incidentally revealed significant bilateral multicystic ovarian enlargement (right ovary, 5.4 × 3.7 × 3.8 cm; left ovary, 8.1 × 5.1 × 5.5 cm) with physiologic flow on colour Doppler ve-

locimetry (Figure 1). The patient was asymptomatic at presentation.

In the differential diagnosis of bilateral ovarian cystic enlargement, malignancy was considered. Tumor markers were assessed: alpha-fetoprotein (AFP) was elevated at 88.80 IU/mL (Reference interval (RI) 0.50-5.80 IU/mL), while cancer antigen 125 (CA-125) and carcinoembryonic antigen (CEA) were within normal reference ranges. Hematologic analysis revealed a normal complete blood count and mildly elevated hepatic transaminases (alanine aminotransferase 68 U/L (RI 4-34 U/L); aspartate aminotransferase 43 U/L (RI 4-27 U/L)). Endocrinologic workup showed markedly elevated serum β -hCG levels (270 IU/mL), suppressed thyroid-stimulating hormone (TSH) level (0.050 mIU/L, RI 0.1-4.0 mIU/L), and elevated free thyroxine (T4) level (1.65 ng/dL, RI 0.70-1.58 ng/dL). Serum testosterone was not evaluated. Based on these findings, a presumptive diagnosis of HL was established. The patient was counseled regarding the benign and self-limiting nature of HL and advised to report symptoms suggestive of ovarian torsion.

At 18 weeks' gestation, selective fetal growth restriction (sFGR) was diagnosed, with an estimated fetal weight for twin A below the 3rd percentile and a 28% discordance between the twins' estimated fetal weights based on biometric parameters. Both fetuses exhibited normal amniotic fluid indices and Doppler assessments of the umbilical artery (UA) and middle cerebral artery (MCA), with sFGR classified as type I per the Gratacós classification⁴. Fetal genetic analysis via amniocentesis with chromosomal microarray returned normal results for both twins. Weekly ultrasound surveillance was instituted, jointly coordinated by the referring

institution and the Integrated Responsibility Center for Fetal Medicine and Surgery (CRI-MCF). Given the stability of the Doppler parameters, conservative management was adopted.

Follow-up sonography at 23+4 weeks revealed a decrease in ovarian size due to partial regression of the cysts previously described (right adnexa, 6.3 × 2.6 × 3.6 cm; left adnexa, 6.3 × 3.7 × 4.2 cm) (Figure 1). The patient remained asymptomatic, and no virilization or symptoms of hyperthyroidism were reported.

At 26+6 weeks' gestation, progression to sFGR Type II was observed, with absent end-diastolic flow in the umbilical artery of the growth-restricted twin. Additionally, early signs of TTTS were detected, namely a marked discrepancy in the deepest vertical pocket (DVP) of amniotic fluid between the twins. In the context of rapid hemodynamic deterioration – characterized by reversed end-diastolic flow in the umbilical artery, reversed a-wave in the ductus venosus, and non-reassuring cardiotocography findings – it was decided to proceed with delivery at 27 weeks and 1 day via cesarean section.

Two live female neonates were delivered. Twin A, weighing 650 g (Apgar scores 6, 8, and 8 at 1, 5, and 10 minutes, respectively), died on postnatal day six due to complications of extreme prematurity. Twin B, weighing 790 g (Apgar scores of 7, 8, and 9 at 1, 5, and 10 minutes, respectively), demonstrated a favorable clinical trajectory, with appropriate growth and neurological development observed at one month of life. No signs of virilization were observed. Placental histopathological examination was consistent with a monochorionic-diamniotic immature placenta, notably with abnormal anastomosis consistent with TTTS.

Maternal clinical reassessment at four weeks postpartum confirmed complete resolution of the bilateral ovarian cysts, corroborating the self-limiting nature of hyperreactio luteinalis (Figure 1).

DISCUSSION

Selective fetal growth restriction (sFGR) in monochorionic twin pregnancies presents a complex clinical challenge due to the shared placental architecture and the inherent presence of intertwin vascular anastomo-

ses, which create the substrate for unequal placental sharing. The Gratacós classification stratifies sFGR into three types based on umbilical artery (UA) Doppler velocimetry in the smaller twin: type I (normal end-diastolic flow), type II (persistent absent/reversed end-diastolic flow), and type III (intermittently absent/reversed flow)^{6,7}. While type I sFGR generally has a favorable prognosis under expectant management, types II and III carry a significantly worse prognosis and often necessitate consideration of fetal therapy^{1,8}. Early-onset sFGR, defined as diagnosis before 24 weeks of gestation, poses a particularly poor prognosis, with significantly elevated risks of intrauterine fetal demise, perinatal morbidity, and neurodevelopmental impairment^{2,3}.

Superimposed twin-to-twin transfusion syndrome (TTTS) may further complicate 27% of early-onset sFGR cases, significantly compounding fetal compromise and adverse perinatal outcomes. Driven by unbalanced intertwin transfusion through placental vascular anastomoses, TTTS is characterized by oligohydramnios and hypovolemia in the donor twin and polyhydramnios with cardiovascular overload in the recipient. Its coexistence with sFGR reflects profound placental pathology and necessitates close fetal surveillance to detect progressive hemodynamic deterioration and determine the optimal timing of intervention^{2,3}.

Our case involved early-onset sFGR (diagnosed <24 weeks) with progression from type I to type II, ultimately leading to iatrogenic preterm delivery at 27+1 weeks. This clinical course is consistent with existing literature, which suggests that approximately one-third of Type I cases evolve into more severe forms of sFGR, underlining the importance of close surveillance⁹. In parallel, early signs of TTTS emerged at 26+6 weeks' gestation, reflecting an evolving intertwin circulatory imbalance and advancing placental dysfunction.

Concurrently, our patient presented with bilateral multicystic ovarian enlargement during routine ultrasound evaluation, with imaging and biochemical features suggestive of hyperreactio luteinalis (HL). HL is a rare but recognizable cause of bilateral adnexal masses in pregnancy, with around 130 cases reported in the literature to date^{5,10}. It is characterized by cystic ovarian enlargement, typically exhibiting a distinctive

“spoke-wheel” sonographic appearance accompanied by physiologic flow on colour Doppler velocimetry. This morphology reflects exaggerated luteinization of the theca interna cells, driven by elevated or abnormally sensitized responses to human chorionic gonadotropin (β -hCG)⁴. Biochemical hallmarks frequently include markedly increased β -hCG concentrations, transient hyperthyroidism, and varying degrees of maternal hyperandrogenism.

Despite its benign nature and typical postpartum resolution, HL is frequently misdiagnosed as an ovarian malignancy, leading to unnecessary surgical intervention in up to 40% of reported cases⁵. Distinguishing features that favor HL over neoplastic pathology include bilaterality, absence of solid components, lack of papillary projections, and the presence of normal Doppler perfusion¹¹.

The present case underscores the clinical value of a conservative, non-operative approach in an asymptomatic patient, guided by consistent imaging characteristics and supportive biochemical findings, including markedly elevated β -hCG and suppressed TSH. Unfortunately, specific quantification of serum androgens was not performed, limiting a more detailed characterization of the hyperandrogenic profile. Nonetheless, the spontaneous postpartum resolution of ovarian enlargement further corroborated the diagnosis and reflects the natural history of HL. Endocrinologic reassessment at delivery, although not mandatory, may have provided additional diagnostic support. Confirmation of the transient nature of the biochemical abnormalities would have further strengthened the diagnosis of HL while helping to exclude alternative endocrine pathology.

The clinical implications of HL extend beyond diagnostic confusion. HL has been associated with maternal complications including preeclampsia, hyperemesis and virilization⁴. For the fetus, growth restriction and preterm delivery have been described, although the pathophysiological connection remains poorly understood^{4,5}. The co-occurrence of HL and sFGR in monochorionic twin pregnancies, as observed in the present case, has only rarely been described in the literature^{5,10}. A limited number of reports, such as those by Sienas et al. and Takeda et al., document HL in the context of monochorionic twin gestations complicated by

TTTS or preeclampsia, raising the possibility that HL may serve as a clinical surrogate marker of impaired placentation^{12,13}.

The overlapping pathophysiology between HL and placental dysfunction warrants further investigation. One proposed mechanism is that the exaggerated production or heightened sensitivity to β -hCG seen in HL may contribute to dysregulated placental vasculogenesis and villous development. These alterations are central to the development of sFGR, TTTS, and preeclampsia, all of which are characterized by varying degrees of placental dysfunction. Moreover, increased hCG levels have been implicated in altered maternal vascular adaptation and endothelial dysfunction, further supporting a potential link between HL and hypertensive disorders of pregnancy^{4,12,13}.

The intersection of early-onset sFGR, early signs of TTTS and HL in this case underscores the critical need for multidisciplinary management. The rarity of this clinical constellation, coupled with the potential for misdiagnosis and adverse outcomes, emphasizes the importance of maintaining a high index of suspicion for HL in pregnant patients with multicystic ovarian masses and elevated β -hCG.

In conclusion, this case exemplifies the unique diagnostic and management challenges posed by the co-occurrence of early-onset sFGR and HL in a monochorionic twin pregnancy. It reinforces the role of careful clinical surveillance, the value of conservative management in HL, and the need for individualized decision-making based on fetal Doppler trends and maternal condition. Future studies are warranted to elucidate the potential mechanistic link between HL and placental dysfunction and to better define the prognostic implications of HL in the context of monochorionic pregnancies.

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AUTHORS' CONTRIBUTION

Joana Gomes Augusto: Conception, design, writing, reviewing and final editing of the article. Maria Fedchenko, Joana Torres Silva, Sandra Batista, Carla Duarte: Critical review of article content and final approval of the version to be published.

CONFLICTS OF INTEREST

Authors declare they have no conflicts of interest.

INFORMED CONSENT

The patient has provided written informed consent for publication.

CORRESPONDENCE TO:

Joana Gomes Augusto
E-mail: joana.gomes.augusto@gmail.com
<https://orcid.org/0009-0004-2732-3616>

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