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### Authors

Sienas, Laura  
Miller, Trevor  
Melo, Juliana  
[et al.](#)

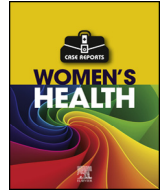
### Publication Date

2018-07-01

### DOI

10.1016/j.crwh.2018.e00073

Peer reviewed



# Hyperreactio luteinalis in a monochorionic twin pregnancy complicated by preeclampsia: A case report

Laura Sienas<sup>a,\*</sup>, Trevor Miller<sup>b</sup>, Juliana Melo<sup>c</sup>, Herman Hedriana<sup>c</sup>

<sup>a</sup> Department of Obstetrics and Gynecology, University of Washington, 1959 NE Pacific Street, Box 356460, Seattle, WA 98195, USA

<sup>b</sup> Department of Obstetrics and Gynecology, Kaiser Permanente San Leandro, 2500 Merced St, San Leandro, CA 94577, USA

<sup>c</sup> Department of Obstetrics and Gynecology, University of California Davis, 2315 Stockton Blvd, Sacramento, CA 95817, USA

## ARTICLE INFO

### Article history:

Received 9 June 2018

Received in revised form 3 August 2018

Accepted 8 August 2018

Available online xxxx

### Keywords:

Adnexal mass

Pregnancy

Hyperandrogenism

Preeclampsia

Twin-twin transfusion syndrome

## ABSTRACT

Hyperreactio luteinalis (HL) is a rare benign complication of pregnancy that is characterized by progressive ovarian enlargement and hyperandrogenism. We present a case of a 30-year-old woman with a spontaneous monochorionic diamniotic twin pregnancy who presented with early-onset preeclampsia, concern about possible twin-twin transfusion syndrome, and bilateral enlarged ovarian masses. Both ovaries had multiple thin-walled unilocular cysts; one ovary measured  $17.9 \times 17.5 \times 9.1$  cm and the other  $12.5 \times 11 \times 12.3$  cm. After extensive counseling, the patient underwent an uncomplicated dilation and evacuation. Postoperative assessment indicated elevated androgen levels, which spontaneously resolved, supporting the clinical diagnosis of HL. It is important to consider HL in the differential diagnosis of adnexal masses in pregnancy. HL spontaneously regresses after delivery and is managed expectantly. HL has been associated with gestational trophoblastic disease, multiple gestations, preeclampsia, and twin-twin transfusion syndrome.

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## 1. Introduction

The incidence of ovarian masses in pregnancy is rare, complicating 1–2% of all pregnancies [1]. The differential diagnosis is vast and some masses require intervention during pregnancy. Hyperreactio luteinalis (HL) is a rare but benign condition. Its hallmarks include bilateral, marked cystic enlargement of the ovaries with associated overproduction of ovarian androgens. We present a case of a patient with a monochorionic diamniotic twin pregnancy, fetal anomalies, early-onset preeclampsia, concern for twin-to-twin transfusion syndrome (TTTS) and enlarging ovarian masses. The uniqueness of this case is the simultaneous association of TTTS, HL and preeclampsia. Our review of the literature suggested that a trifecta of this nature has not been previously reported.

## 2. Clinical Case Report

A 30-year-old woman, gravida 2 para 1001, presented for ultrasound assessment of her spontaneous monochorionic diamniotic twin pregnancy. She had had a previous uncomplicated term pregnancy and no significant medical history. At 16 weeks' gestation, a fetal anatomy evaluation indicated no apparent anomalies and normal bilateral adnexa. Two weeks later, an ultrasound showed twin A with a large ventricular

septal defect but normal amniotic fluid volume; an umbilical artery Doppler study (UAD) was also normal. Twin B had bilateral ventriculomegaly with a non-visualized corpus callosum and oligohydramnios; UAD showed absent end diastolic flow (AEDF). There was 41% discordance between the twins' estimated fetal weights based on biometric parameters. The patient was counseled about the possibility of twin-twin transfusion syndrome (TTTS). A right complex ovarian mass measuring  $7 \times 5.7 \times 7.5$  cm (Fig. 1) was noted by the uterine fundus. To rule out ovarian malignancy, a cancer antigen125 was drawn and was normal ( $<35$ /value). The beta human chorionic gonadotropin level was  $>200,000$ . She had a normal complete blood count and liver enzymes. A basic metabolic panel was within normal limits except for mild hyponatremia at 130 mEq/L.

At 19 weeks' estimated gestational age, the patient complained of increasing abdominal pain. Given new-onset pain, ultrasound and MRI were performed for evaluation and gynecology oncology consultation was planned. The ovaries were markedly enlarged, with numerous small follicular cysts (right adnexa  $6.8 \times 10.1 \times 9.4$  cm and left adnexa  $7 \times 12 \times 10$ cm) and concurrent ascites was noted. Twin A had normal amniotic fluid volume and UAD. Twin B had anhydramnios, a non-filling bladder, and persistent AEDF. At this point the patient declined intervention despite being counseled that the prognosis was dire.

The patient returned four days later with shortness of breath and lower-extremity edema. She was found to have new-onset hypertension but her preeclampsia work-up was only significant for proteinuria

\* Corresponding author at: 1959 NE Pacific Street, Box 356460, Seattle, WA 98195, USA.  
E-mail address: [lsienas@uw.edu](mailto:lsienas@uw.edu) (L. Sienas).

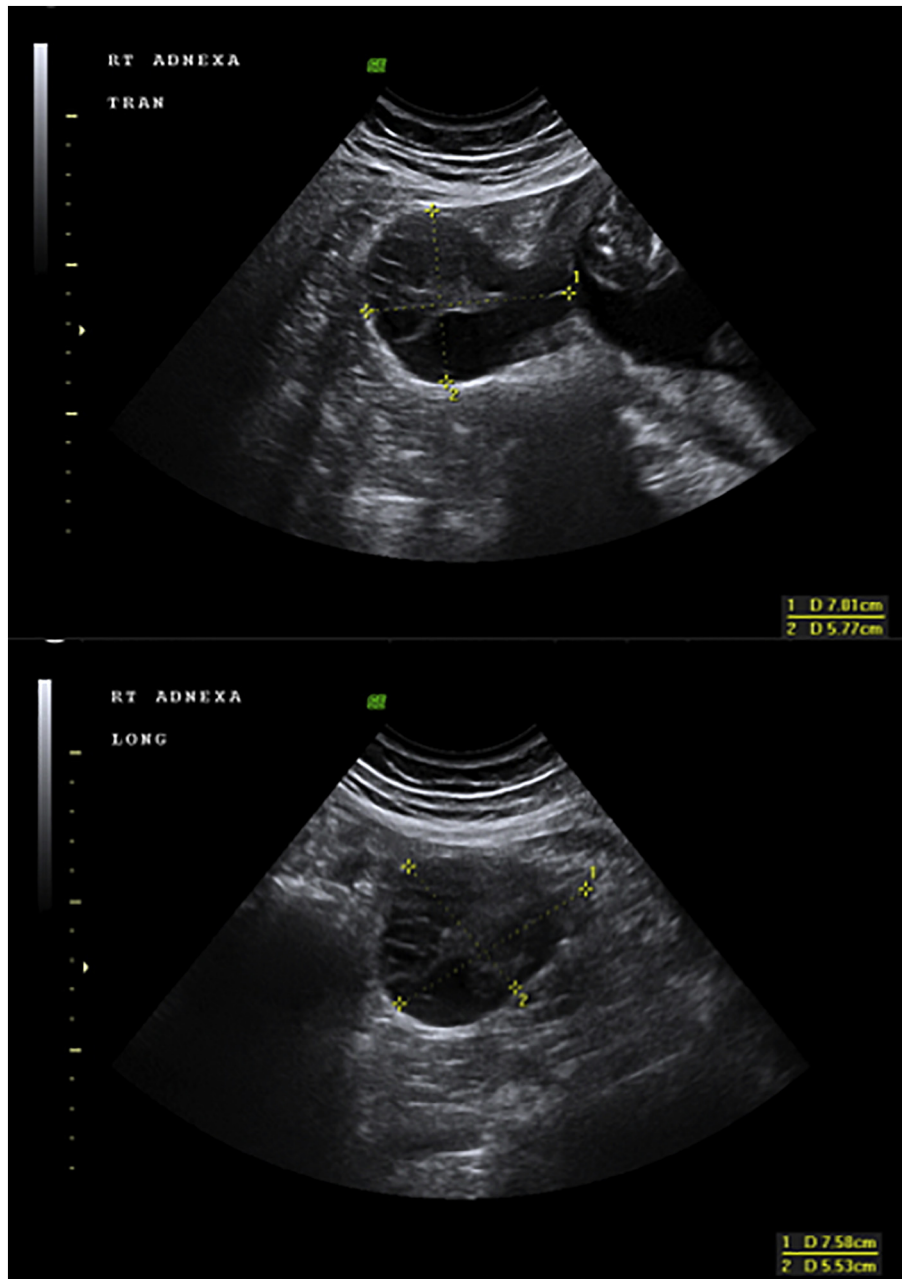


Fig. 1. Ultrasound scan of the right ovary at 18 weeks' gestation. Upper image: Transverse plane. Lower Image: Longitudinal plane.

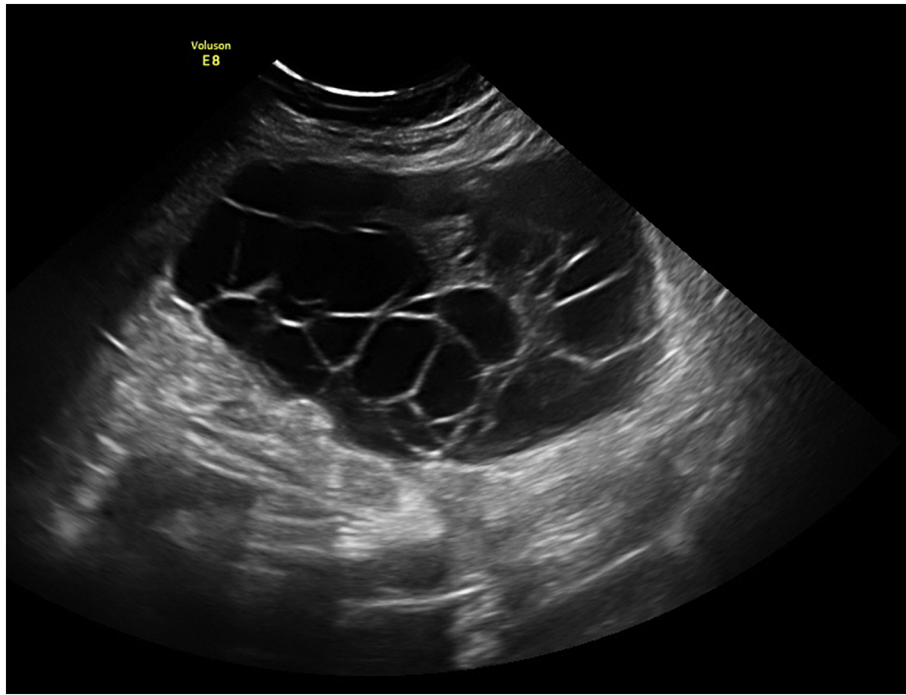
(1958 mg/24 h). Due to persistent hypertension, she met diagnostic criteria for preeclampsia without severe features. After extensive counseling about her evolving preeclampsia and risk of respiratory distress due to abdominal distention, and in light of the fetal anomalies and TTTS, the patient elected for termination of pregnancy via dilation and evacuation (D&E). At 19 5/7 weeks, a standard D&E was performed under ultrasound guidance without complications. Pathology examination confirmed TTTS characterized by 65% discordant biometrics, marked pallor in the donor twin and plethoric recipient twin. Both fetuses were male. Placenta pathology was consistent with a monochorionic-dichorionic immature placenta, notably with abnormal anastomosis consistent with TTTS.

On postoperative day one, she was normotensive and complained only of abdominal fullness. On ultrasound, markedly enlarged ovaries were noted, the left measuring  $17.9 \times 17.5 \times 9.1$  cm and the right  $12.5 \times 11 \times 12.3$  cm (Fig. 2). The differential diagnoses included ovarian hyperstimulation syndrome (OHSS) and hyperreactio luteinalis (HL). An

androgen panel revealed elevated levels of androstenedione at 15.9 ng/mL (0.26–2.14 ng/mL) and testosterone at 11.78 ng/mL (<0.2–0.73 ng/mL), but normal dihydroepiandrosterone (DHEA) at 1.79 ng/mL (1.33–7.78 ng/mL). She did not exhibit any maternal virilization. Given her characteristic ultrasound findings and lack of biochemical features supporting OHSS, our final diagnosis was HL. The decision was made to manage her course expectantly. The androgen panel was repeated one month later and showed a decline in androstenedione to 9.62 ng/mL (0.3–2.5 ng/mL) and testosterone to 2.84 ng/mL (0.02–0.45 ng/mL). The patient was asymptomatic and no longer complained of abdominal fullness.

### 3. Discussion

The differential diagnoses of an ovarian mass in pregnancy may include corpus luteum cyst, follicular cyst, endometrioma, malignancy, luteoma and OHSS. OHSS and HL have similar ultrasound

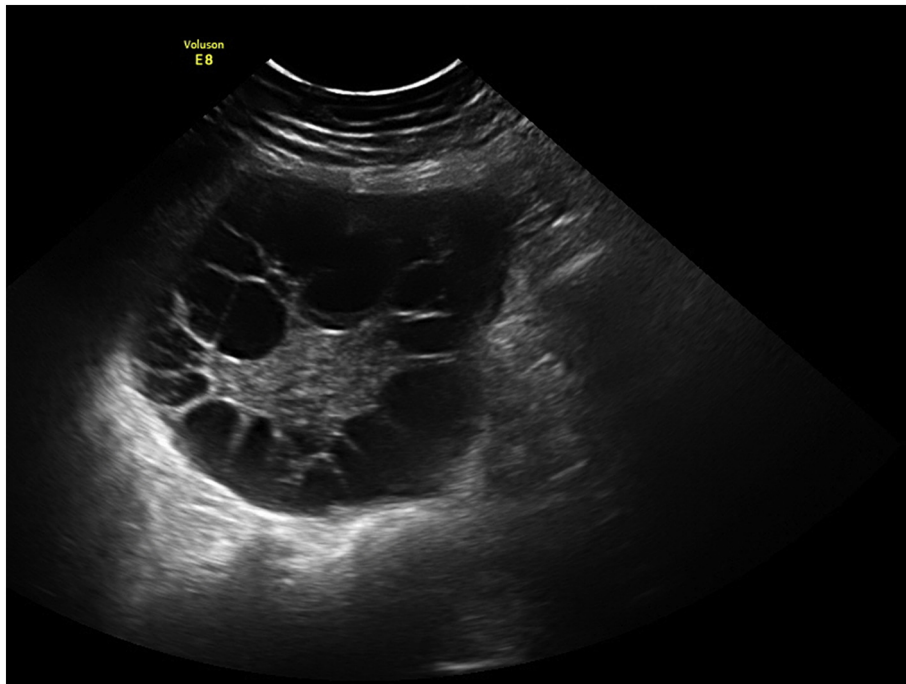


**Fig. 2.** The enlarged adnexa seen on postoperative day 1 in the patient with hyperreactio luteinalis.

characteristics, principally in the form of a “spoke-wheel” pattern with many thin-walled small simple cysts [2] (Fig. 3). Our initial working diagnosis for the ovarian masses was OHSS with evidence for TTTS. OHSS is characterized by ovarian enlargement >10 cm, ascites, pleural effusion, electrolyte abnormalities and hemoconcentration [3]. This usually presents in the first trimester, and is associated with fertility treatments. Spontaneous cases have been reported [3, 4] and are thought to be due to hypersensitivity to follicle stimulating hormone. Although differentiation from HL is challenging, OHSS usually has more rapid fluid shifts, occurs earlier in pregnancy, and has no evidence of biochemical

hyperandrogenism. Due to the elevated androgen levels and spontaneous conception, the patient met the diagnostic criteria for HL.

The exact etiology of HL is unknown but the condition has been associated with very high serum  $\beta$ -HCG levels in association with gestational trophoblastic disease and multiple gestations [3, 4]. In our literature search, approximately 100 cases have been reported with normal pregnancy [2], among which only 8 cases were with multiple gestations. HL is usually an incidental finding during cesarean section; in most cases, the patient is asymptomatic without evidence of maternal or fetal virilization [5]. Virilization symptoms were reported in 15–20%



**Fig. 3.** Characteristic spoke-wheel pattern of multiple ovarian cysts in the patient with hyperreactio luteinalis.

of women [2, 4]; other symptoms included ascites, abdominal pain, pelvic congestion, and ovarian torsion [4]. Our patient manifested some of these symptoms without virilization.

Hypertensive disorders, including the early development of preeclampsia, HELLP syndrome and eclampsia, have been described in patients with HL [5]. In a retrospective study of 31 HL patients, 29% developed a hypertensive disorder [4]. It has been hypothesized that the elevation of  $\beta$ -HCG could be due to poor placentation in pregnancy, which may be a risk factor for the development of preeclampsia [5]. This risk may be compounded in monochorionic twins with TTTS. Lynn et al. reported 2 cases of TTTS associated with HL [4]; Takeda reported 4 cases of HL with severe TTTS [6]. Although the pathophysiology is not understood, there appears to be an association between TTTS and HL. Given these associations, we speculate that the monochorionic placentation and abnormal distribution of blood flow that caused the TTTS in the presence of HL resulted in early-onset preeclampsia.

It is important to consider HL in the differential diagnosis of an ovarian mass in pregnancy, as misdiagnosis may lead to unnecessary surgical intervention. With expectant management, HL will spontaneously resolve in the postpartum period. Patients should be counseled about the low recurrence risk [2, 4] in future pregnancies, as only a few cases have been reported in the literature [7–10]. However, this case brings into light an association of TTTS, HL, and early-onset preeclampsia. This case demonstrates the difficulty of sorting out differential diagnoses in a rapidly evolving disease that can cause significant maternal-fetal complications.

#### Contributors

Laura Sienas cared for the patient, wrote the manuscript, and participated in revising it.

Trevor Miller cared for the patient, conceived the idea for the case report, and participated in revising and editing the manuscript.

Juliana Melo cared for the patient, and participated in revising and editing the manuscript.

Herman Hedriana cared for the patient, and participated in revising and editing the manuscript.

#### Conflict of Interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

#### Funding

No funding was sought or secured in relation to this case report.

#### Patient Consent

Obtained.

#### Provenance and Peer Review

This case report was peer reviewed.

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