

Hyperreactio Luteinalis with early-onset HELLP syndrome: A case report

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ABSTRACT

Introduction: Hyperreactio Luteinalis (HL) is a rare benign condition in pregnancy which is characterized by bilaterally multicystic ovarian enlargement containing theca lutein cysts caused by increased production of hCG. HL is mostly associated with hydatidiform mole and multiple pregnancies.

Case Report: We report a unique case of hyperreactio Luteinalis (HL) in spontaneous singleton pregnancy with elevated level of human chorionic gonadotropin (hCG) and alpha-fetoprotein (AFP) for who referred to our center for high blood pressure and proteinuria which subsequently developed early-onset HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count) at 18 weeks of pregnancy. Termination of pregnancy was considered and a patient passed a normal dead fetus. Placental histology showed evidence of hypoperfusion with focal villous infarction and ischemic changes without evidence of trophoblastic abnormalities.

Conclusion: Hyperreactio luteinalis associating with high level of hCG in second trimester can be consequence of inadequate trophoblast invasion and may be a risk factor for early onset HELLP syndrome.

Key words: Hyperreactio Luteinalis, Preeclampsia, HELLP Syndrome

Introduction:

Hyperreactio Luteinalis (HL) is a rare benign condition in pregnancy that can occur at any stage. These benign ovarian lesions are characterized by bilaterally multicystic ovarian enlargement containing theca lutein cysts caused by increased production of hCG (1). HL is mostly associated with hydatidiform mole and multiple pregnancies. Most pregnant women with HL are asymptomatic and enlarged ovaries who are usually accidentally recognized by routine ultrasound examination (2).

HL should be differentiated from ovarian hyperstimulation syndrome (OHSS). OHSS almost exclusively occurs in patients following fertility treatment; however, very rarely it occurs in

spontaneous singleton pregnancies, particularly in polycystic ovarian syndrome (PCOS). Iatrogenic OHSS is diagnosed immediately following conception but HL which is an exaggerated ovarian luteinization in response to high level of hCG that is often diagnosed later in pregnancy (3,4). A few cases of HL occurring in normal singleton pregnancies have been reported and some of those cases were associated with hyperemesis gravidarum, hyperthyroidism, hirsutism, preeclampsia, or HELLP (3). We present a case of HL with markedly elevated levels of hCG in the early 2nd trimester of pregnancy which developed HELLP syndrome subsequently.

Case Report:

A 26 - year - old woman primigravid was referred to our hospital for high blood pressure and proteinuria at 18 week's gestational age. Her past history was unremarkable and she had a spontaneous conceived singleton pregnancy. In advance, she developed persistent headache and epigastric pain especially at the right upper quadrant. Her blood pressure (BP) increased from 150/90mmHg to 160/110mmHg and urinalysis showed a two episodes of 3+ proteinuria. Abdominal ultrasonography examination revealed a living normal sized fetus, anterior placenta with thickness of 50mm, and bilateral multicystic ovarian mass+ without any solid component and ascites (right ovary: 149×107×77mm; left ovary: 132×68×57mm) (Figures 1 and 2).

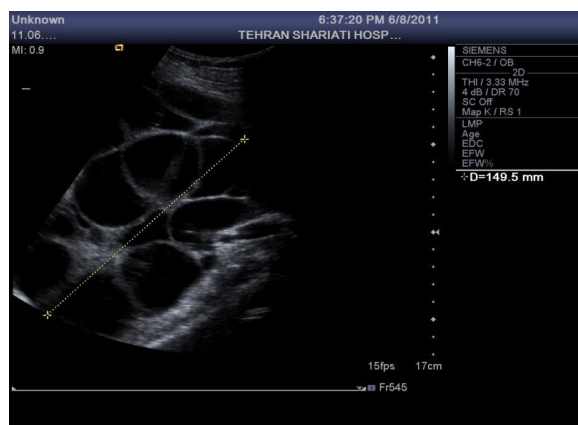


Figure 1. Enlarged multicystic right ovary in hyperreactio luteinalis.

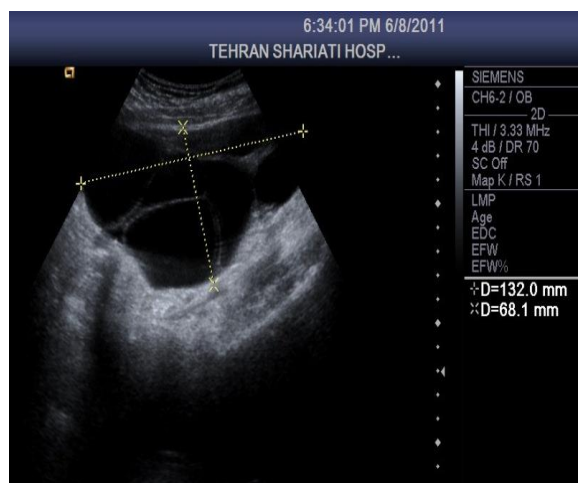


Figure 2. Enlarged multicystic left ovary

Initial laboratory testing showed platelet (PL, $96 \times 10^9/L$) count and levels of hemoglobin (Hb; 9.6 g/dl), hematocrit (HCT; 27.3%), blood urea nitrogen (BUN; 9 mmol/L), creatinine (cr; 0.8 mg /dl), aspartate transaminase (AST;109 U/L), alanine transaminase (AIT; 113 U/L), Lactate dehydrogenase (LDH; 971 U/L), total bilirubin (1.2 mg/dl), and direct bilirubin (0.4 mg/dl). The peripheral blood smear (PBS) examination showed 1% schistocytes - The quadruplet test showed elevated levels of hCG (236×10^3 IU/L; 4.95 MoM) and alpha- fetoprotein (AFP; 137.4 IU/ml; 5.13 MoM). The fibrinogen level (240 mg/dl), prothrombin time (PT; 12.6s), active partial thrombin time (APTT; 25s), electrolytes (Na; 137 mmol/L, K; 4.3 mmol/L), and blood sugar (BS; 116mg/dl) were within normal limits. Laboratory findings of hemolysis (Hb; 9.6g/dl, T.B; 1.2 mg/dl, LDH; 971 U/L, schistocyte; 1% in PBS), low platelet level ($96 \times 10^9/L$), elevated liver enzymes (ALT; 113 U/L, AST;1.9 U/L), and hypertension were consistent with severe preeclampsia/HELLP syndrome. Pregnancy was terminated with administration of misoprostol 400 μ g intravaginal. - she passed a looking normal dead fetus after 4 hours; 300gr, 18 cm and placenta 18×12×5 cm was unremarkable (Figure 3).



Figure 3: Looking normal dead fetus with hypertrophic placenta

Placental histology showed evidence of hypoperfusion with focal villous infarction and ischemic changes without evidence of infection or trophoblastic abnormalities. The blood pressure and abnormal laboratory findings returned to normal level after a week. The patient was advised to check

antiphospholipid antibodies, thrombophilia factors, and tumor markers 6 weeks later which were within normal limit. At approximately 10 weeks of postpartum, hCG levels returned to normal and both ovaries at 12 week postpartum appeared normal in size.

Conclusion:

The etiology of hyperreactio Luteinalis (HL) is unknown. However, it is believed that production of high concentration of hCG and increased ovarian sensitivity lead to theca Lutein cyst formation. It is uncommon in pregnancies not associated with trophoblastic disease (1,2). Bilateral multicystic ovarian mass may mimic spontaneous OHSS.

This condition occurs particularly with induction of ovulation in PCOS.

Ovarian enlargement with concomitant fluid shifts such as ascites, pleural effusion, and hemoconcentration has been reported to be typically rapid and early in OHSS (3,4).

This patient had no history of induction of ovulation and showed no hemoconcentration in laboratory data or ascites in ultrasonography suggestive for OHSS. When enlargement of bilateral ovaries is found during pregnancy, it is important to differentiate HL from malignant ovarian tumors to avoid unnecessary surgery. HL is mostly bilateral and found incidentally at the time of cesarean section. However, HL may be present during any trimester of pregnancy as an abdominal mass or acute abdominal pain, the natural course is postpartum regression (4,5).

In this case, we observed high hCG levels and normal ranges of ovarian tumor markers with no evidence of malignancy in imaging study that gradually resolved 3 months of postpartum. Five cases of HL associated with pregnancy induced hypertension (PIH) and one case with HELLP syndrome was found in MEDLINE search. All of these cases had HL with PIH in normal pregnancy that presented at the third trimester (6-11), while the present case of HL with HELLP occurred as early onset at second trimester of pregnancy. The elevation of hCG derived from placenta and AFP in a pregnancy could be marker of poor placental invasion, which leads to development of preeclampsia. Observation of hCG levels during the

second trimester has been shown to be useful in identifying pregnancies that will develop preeclampsia (12). Placental abnormalities and many types of birth defects are associated with AFP elevation. In addition, these pregnancies are at incremental risk for a variety of subsequent adverse pregnancy outcomes such as preeclampsia, fetal growth restriction, oligohydramnios, placental abruption, preterm membrane rupture, preterm birth, and even fetal death (13). Similar to these studies, elevated hCG and AFP in this case predicted adverse pregnancy outcome such as HELLP syndrome. Although, the risk of partial molar gestation was considered to be remote based on findings from sonography, the conceptus was elected to undergo pathology investigation and autopsy for evaluation of partial molar gestation. Partial molar gestation is associated with triploidy, but in this case the fetus was normal without evidence of trophoblastic abnormalities.

The limitations of the study were that there was no evaluation of other maternal serum markers and angiogenic factors to predict preeclampsia and amniocentesis to perform karyotyping.

In conclusion, HL may be a predictor of early-onset preeclampsia and HELLP syndrome in pregnancy. The occurrence of HELLP syndrome before 20 weeks of gestation is extremely rare. This condition has been reported in only few cases, and always in conjunction with other comorbidities such as fetal triploidy or antiphospholipid syndrome. Early presentation, such as in our case, may result in severe maternal morbidity and mortality especially if HELLP syndrome is not suspected.

Awareness, early detection, intensive maternal monitoring, and early intervention may be lifesaving. Therefore, this case may guide obstetricians in considering the diagnosis of HELLP syndrome in women presenting HL with clinical manifestations or laboratory abnormalities which are consistent with this condition even 20 weeks before gestation.

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Hyperreactio Luteinalis با سندرم HELLP در هفته ۱۸ بارداری (گزارش یک مورد)

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چکیده

مقدمه: *Hyperreactio Luteinalis* یک وضعیت خوش‌خیم نادر در دوران بارداری است و با تخمدان بزرگ چند کیستی ناشی از افزایش تولید هورمون *hCG* مشخص می‌گردد. *HL* اغلب مرتبط با مول و چندقلویی است.

معرفی بیمار: گزارش یک مورد منحصر به فرد در یک حاملگی تک قلو با بارداری خودبه‌خودی با سطح بالای آلفا فیتوپروتئین (*AFP*) و گنادوتروپین جفتی انسانی (*hCG*) است که به علت فشارخون بالا و پروتئینوری به مرکز ما ارجاع شده بود. متعاقباً بیمار دچار سندرم *HELLP* (همولیز، افزایش آنزیم‌های کبدی و تعداد پلاکت پایین) با شروع زودرس در هفته ۱۸ بارداری گردید. ختم حاملگی در نظر گرفته شد و او یک جنین مرده طبیعی را دفع کرد. بافت شناسی جفت شواهد کاهش خون‌رسانی با انفارکتوس پرزی و تغییرات ایسکمیک کانونی بدون اختلالات تروفوبلاستی را نشان داد.

نتیجه‌گیری: *HL* مرتبط با افزایش سطح هورمون *hCG* در سه ماهه دوم می‌تواند ناشی از تهاجم ناکافی تروفوبلاست باشد و ممکن است یک عامل خطر برای سندرم *HELLP* با شروع زودرس باشد.

کلیدواژه‌ها: *Hyperreactio Luteinalis*، پرهاکلامپسی، سندرم *HELLP*

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