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A case of hyperreactio lutenalis complicated by mirror syndrome presenting with characteristic ultrasound findings

Ryoichi Asaka1, Miyuka Murasato1, Akiko Higuchi1, Yusuke Yokokawa1, Yasuhiro Tanaka1, Motoki Ono1, Chiho Fuseya1, Norihiko Kikuchi1, Tsutomu Miyamoto1, Makoto Kanai2
1. Obstetrics and Gynecology, Shinshu University, Matsumoto, Nagano Prefecture, Japan.
2. School of Health Sciences Department of Family and Child Nursing, and Midwifery, Shinshu University, Matsumoto, Nagano Prefecture, Japan

SHINSHU UNIVERSITY

Abstract

[Introduction]Hyperreactio luteinalis (HL) is a benign condition characterized by bilateral, multilocular enlargement of the ovaries due to hCG stimulation during pregnancy. We report a case of HL associated with Mirror Syndrome, which is characterized by fetal hydrops, maternal edema, and placental edema.[Case Report]A 29-year-old woman, gravida 2 para 0, became pregnant through frozen-thawed embryo transfer. At 12 weeks of pregnancy, cystic hygroma was detected by her previous physician. At 15 weeks of pregnancy, both of her ovaries were found to be enlarged to 9 cm, and her serum hCG level was elevated to more than 1,000,000 mIU/mL. Although malignancy was ruled out by MRI, further evaluation and treatment were recommended, and she was transferred to our hospital at 16 weeks of pregnancy.Ultrasound examination revealed fetal hydrops, and the placenta appeared edematous and thickened. Both ovaries were enlarged to 10 cm with a multilocular structure, showing a "spoke-wheel appearance," leading to a diagnosis of HL. The mother showed elevated blood pressure and generalized edema, and blood tests revealed hemoglobin at 8.2 g/dL, hematocrit at 25.1%, indicating hemodilution, and markedly elevated serum hCG at 1,322,000 mIU/mL, raising suspicion of Mirror syndrome. Two days after her transfer, intrauterine fetal death occurred, and the fetus was delivered the following day, but the placenta did not expel naturally.Due to worsening maternal hypertension and edema, as well as the deterioration of her general condition, a uterine evacuation was performed two days later to remove the placenta. After the procedure, her condition stabilized, and her serum hCG level dropped to 17,047 mIU/mL on the 8th postoperative day, allowing for discharge. Her ovarian condition is being monitored on an outpatient basis.[Conclusion]HL can be misinterpreted as an ovarian tumor requiring surgical removal due to its rapid enlargement during pregnancy, but if diagnosed based on typical clinical course and imaging, conservative management is recommended as it spontaneously regresses. It is important to note that, as in this case, hyperhCGemia associated with Mirror syndrome can also be a trigger for the development of HL.

Introduction

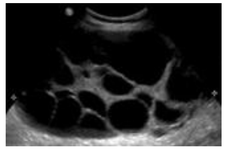
Hyperreactio Luteinalis （HL）

【Definition】
A condition characterized by **bilateral ovarian enlargement due to the formation of multilocular cysts induced by hCG stimulation.**
【Clinical Symptoms】
Asymptomatic 28 %, Abdominal pain 52 % ,
Nausea and vomitting16 %
【Ultrasonographic Findings】
Bilateral ovarian enlargement
Multiple **cysts clustering over the ovarian stroma**
This pattern has been termed the "**spoke wheel sign**"

Although this condition typically regresses spontaneously after delivery and should be managed expectantly, it is often difficult to differentiate from malignant tumors, and surgical intervention has been performed in more than half of the reported cases.
➡ **Accurate diagnosis and management can help avoid unnecessary invasive procedures.**

Spoke wheel

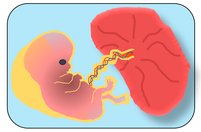




Spoke wheel sign

Mirror Syndorome

【Definition】
A condition characterized by maternal edema and placental edema as a reflection of fetal hydrops, collectively referred to as **"triple edema"**.
【Maternal Clinical Symptoms】
Weight gain 84%, Hypertension 60%, Hemodilution or anemia 51%,
Heart failure 10.6%, Pulmonary edema 8.5%, Renal dysfunction 8.5%
【Fetal Outcomes】Live birth 33%, Fetal death 39%, Neonatal death 23%



Ttriple edema
○Fetal hydrops
○Placetal edema
○Maternal edema



Case presentation

29-year-old woman, G2P0
Height: 165 cm, Pre-pregnancy weight: 62 kg
Past Medical History:
•Lumbar spinal schwannoma
•Uterine myoma
(underwent laparoscopic and hysteroscopic myomectomy two years ago)

In vitro fertilization (IVF) with frozen-thawed embryo transfer.

At 12w1d:
Visited Hospital due to genital bleeding.
Ultrasound : Fetal cystic hygroma
Bilateral polycystic ovary in the mother.

At 15w3d:
MRI: Bilateral ovarian enlargement, with no diffusion restriction in the solid components, suggesting a **diagnosis of HL. (See Images)**

At 15w5d:
Preterm premature rupture of membranes.
400g of genital bleeding.
Transferred to our hospital for further evaluation and treatment.
(See Lab Data and Images)
【Maternal physical findings】
Body temperature 37.3℃ Blood pressure 140/107 mmHg
Heart rate 93 bpm Weight 59.6 kg
Edema is observed in the face and lower legs.

At 16w0d: Intrauterine fetal death
At 16w1d:
Spontaneous labor ensued, and the fetus was delivered.
However, the placenta did not separate spontaneously.
2days after delivery:
Procedure: Placental removal
Intraoperative blood loss: 2,000 g
Transfusion: 4 units of red blood cells and 4 units of fresh frozen plasma.
10days after delivery: Discharge from the hospital.

4month after delivery: **hCG 7mIU/mL. Bilateral ovaries shrinked.**

Lab Data (15w5d)

Biochemistry		
Alb	2.9	g/dL
BUN	6.9	mg/dL
Cre	0.49	mg/dL
UA	3.6	mg/dL
Na	137	mmol/L
K	4.1	mmol/L
Cl	108	mmol/L
CRP	0.07	mg/dL

Blood count		
WBC	11290	/μL
Hb	10.3	g/dL
Hct	30.4	%
Plt	28.7	10^4/μL

Coagulation system		
PT-INR	0.96	
APTT	28.3	sec
FIBG	493	mg/dL
AT-III	89	%

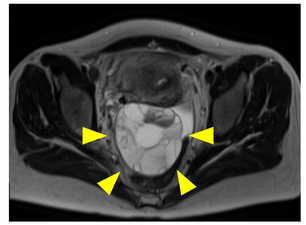
Hormone	
hCG	1322000mIU/mL

Tumor marker	
CA125	21.5 U/mL
CA19-9	< 2.0 U/mL
CEA	2.5 ng/mL

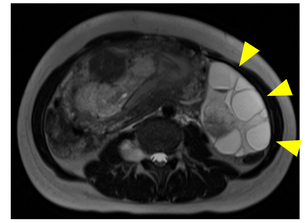
Hemodilution, Abnormally High hCG, Normal tumor maker

Images

15w3d
MRI (T2WI)



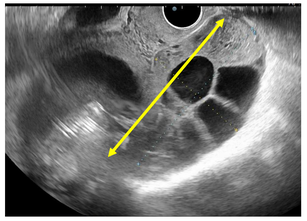
Right Ovary 7cm



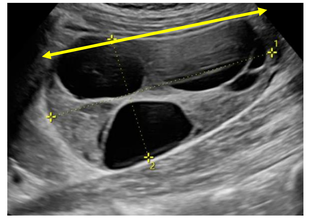
Left Ovary 9cm

MRI demonstrated bilateral multilocular cystic ovarian lesions, with no solid components and no definite evidence of malignancy.

15w5d
Trans vaginal
Ultra Sonograph



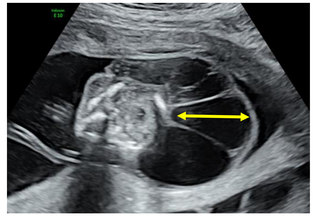
Right ovary 9.9cm



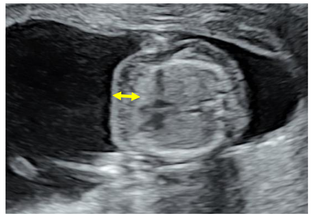
Left ovary 9.7cm

Bilateral ovaries show “Spoke wheel sign”

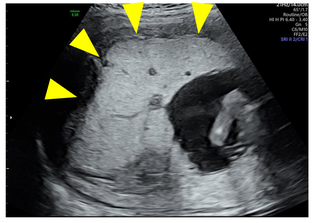
15w5d
Trans Abdominal
Ultra Sonograph



Fetal cystic hygroma



Fetal edema



Placental edema

Discussion

Differential diagnosis of bilateral cystic ovarian masses during pregnancy

OHSS: Ovarian Hyperstimulation Syndrome

	HL	OHSS	Ovarian cancer (Mucinous)
Time of onset	**Anytime in pregnancy**	Early pregnancy	Anytime in pregnancy
Size change	**Enlargement (During pregnancy) Spontaneous regression (After pregnancy)**	Spontaneous regression	**Enlargement**
Blood hCG	Normal～**Abnormally High**	Normal	Normal
Blood concentration	**Hemodilution**	Hemoconcentration	Normal
US findings	Bilateral polycystic ovary **“Spoke wheel sign”**	Bilateral polycystic ovary Ascites	Uni/Bi-lateral polycystic ovary
MRI findings (Restricted diffusion In solid component)	Negative	Negative	**Positive “stained glass pattern”**

If multilocular cystic lesions are observed in both ovaries during pregnancy, hyperreactio luteinalis (HL) can be differentiated by performing blood tests, ultrasonography, and MRI.

Relationship between HL and Mirror syndrome

・This is the first report of HL complicated by Mirror syndrome.
・The pathogenesis of HL remains unclear. However, it is presumed to be associated with strong stimulation by hCG or an over response to hCG.
・HL has frequently been reported in association with trophoblastic disease and twin pregnancies.
・Since both conditions are rare, there is concern that a certain number of cases may have gone undiagnosed.

Conclusion

We experienced a case of HL that was considered to have developed due to high hCG levels associated with Mirror syndrome.

In HL, the ovaries can rapidly enlarge bilaterally during pregnancy; however, if accurately diagnosed, conservative management with expectant observation is possible as spontaneous regression can be anticipated.

When fetal cystic hygroma is observed, maternal evaluation with consideration for the potential development of Mirror syndrome and HL may help prevent unnecessary medical interventions and alleviate excessive anxiety in the patient.

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Conflict of the Interest Disclosure Statement
Name of the Authors： Ryoichi Asaka
Affiliation： Department of Obstetrics and Gynecology, Shinshu University
I have no financial relationships to disclose.