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Case Report

Spontaneous OHSS in Successful Pregnancy Following Medicated Thawed Embryo Transfer Cycle: A Case Report

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Background

Ovarian hyperstimulation syndrome is a disorder associated with exogenous Gonadotropin and is an iatrogenic complication of ovulation induction therapy in ART during the luteal phase and or early stages of pregnancy. Severe OHSS is considered a life-threatening condition and occurs in 0.2%-1.2% of stimulated cycles.

The characteristic pathophysiology of OHSS is due to release of number of vasoactive amines including vascular endothelial growth factor (VEGF) and other pro-inflammatory factors resulting in increased capillary permeability, leakage of fluid from the vasculature, third space fluid accumulation and intravascular dehydration. fatal cases are associated with cerebral infarction, pulmonary thromboembolism, and massive pulmonary oedema.

In literature, sporadic cases of spontaneous OHSS have been reported amongst naturally-conceived pregnancies, and non-pregnant women with primary hypothyroidism, polycystic ovarian disease, molar pregnancies, pituitary adenomas, and in women with follicle stimulating hormone (FSH) receptor mutations.

Even though the condition is extremely rare, spontaneous OHSS can be lethal if not timely diagnosed or tend to be mismanaged due to misdiagnosis.

We report a case of spontaneous ovarian hyperstimulation syndrome in a 39- year-old woman, pregnant after receiving medicated thawed embryo transfer cycle. Although the onset of OHSS was not until 12 weeks of gestation, the corresponding diagnosis was considered in presence of twin pregnancy characterized by elevated β-hCG levels, bilateral enlarged ovaries, ascites, with other physical and biochemical findings suggestive of intravascular depletion.

Case Report

A 42-year-old UAE female with abdominal pain, nausea, and tense abdomen presented to the ER with 9 weeks +5 days DC/DA twins. After post-treatment at Tawam fertility center, she was hospitalized with enlargement of the ovaries, ascites, and a provisional diagnosis of OHSS. She had a diffusely distended abdomen with no tenderness. Her blood tests showed beta-hCG, e2, hgb, platelets, WBC, low urea levels, and normal Haematocrit HTC.

Case report and Infertility Background

The patient experienced secondary infertility for 1.3 years, with a child born in July 2015 following multiple trials of both ivf and fet. The patient had oligomenorrhea and was diagnosed with PCOS according to the 2003 Rotterdam criteria. Hormones included AMH, FSH, LH, E2, and TSH. The patient received an ICSI cycle for male factor, anovulation, and advance age in July 2017.

The patient had a failed medicated FET in January 2018 and a successful pregnancy from medicated FET in May 2018. Oral estradiol valerate (6mg) was started, and when the endometrial thickness was 9mm, vaginal progesterone was administered. and the patient had three blastocyst embryo transfers (Unscreened embryos). The patient had positive pregnancy test 2 weeks post embryo transfer and was discharged from IVF center for early ANC booking after confirming clinical viable pregnancy with twins at 6 weeks. The patient attended ER at 13+4 weeks with complaints of abdominal pain and distension. Abdominal scan showed DC/DA twin-pregnancy and enlarged ovaries with good vascularity and multiple follicular cysts seen. The ovaries measured 17.9 x 12 x 18 cm, with largest cyst measuring 5 x 3.79 cm. Free fluid was seen in the hepatorenal area and a small amount was noted in the pelvic area.

Both ovaries were enlarged with multiple follicular cysts, and there was no obvious fluid in the cul-de-sac. The patient improved and was discharged after receiving IV paracetamol.

The patient returned few days later with low grade fever and the feeling of abdominal distension with no other respiratory or GI complaints. The patient was admitted for medical management and had eventually 1.5 litres of ascitic fluid drained transvaginally under the U/S guidance. She was discharged in better condition and later had Cervical Cerclage at 15+ weeks.

After cerclage, both ovaries were still enlarged with multiple follicular cysts, and adequate doppler flow was seen in both. No obvious fluid was found in the cul-de-sac.

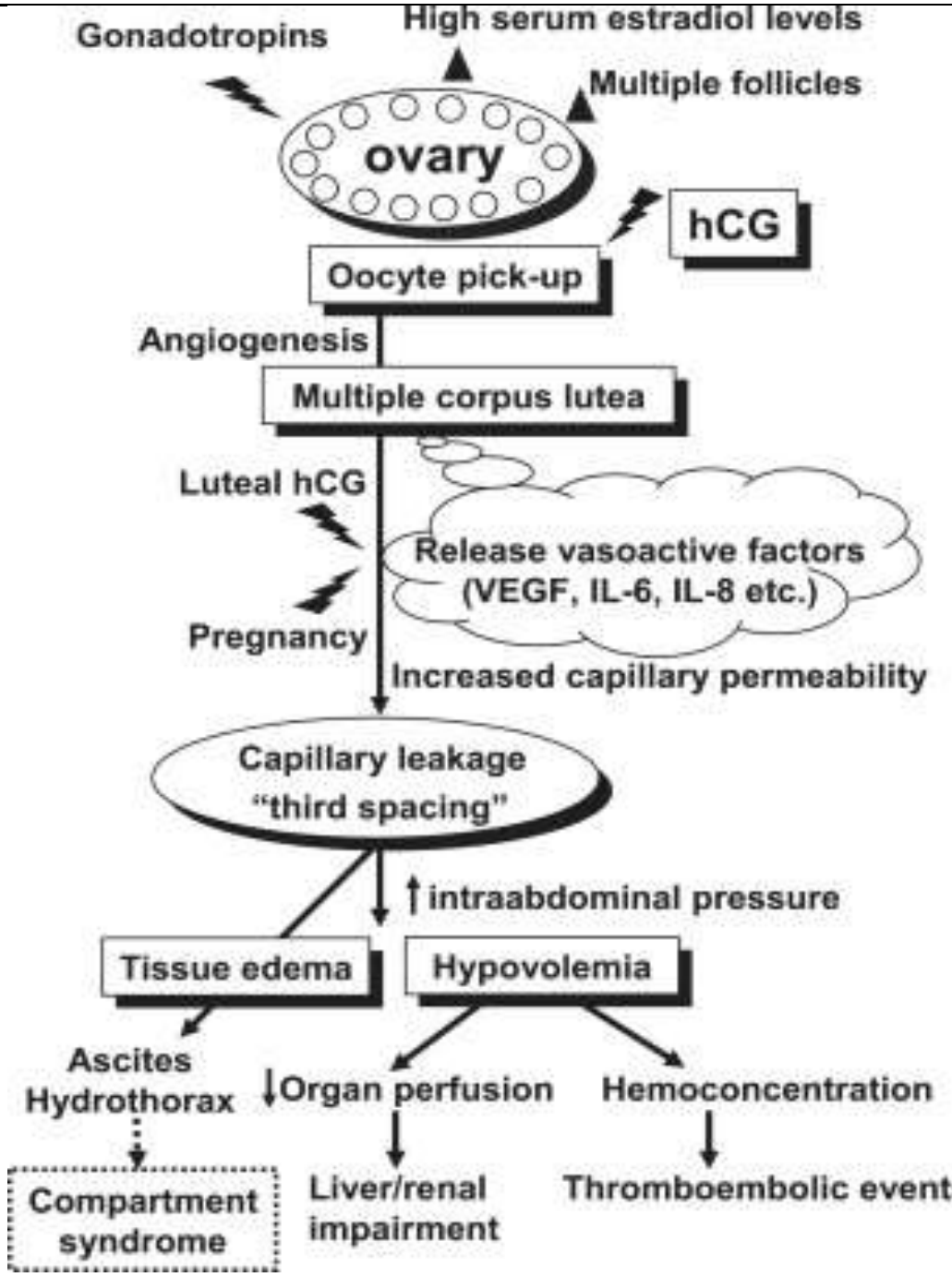
During her ANC visit at 26+ weeks scan, both ovaries were still seen enlarged with multiple clear cysts. The largest cyst size was 6.4x5.1cm and 6.1x4.2cm, while the largest cyst size was 2.7x2.6cm and 2.9x3.0cm. Both ovaries showed good vascularity, again with no evidence of ascitic fluid.

Management

The patient had a preterm labor at 29 weeks plus 3 days gestation following an upper respiratory tract infection, with spontaneous vaginal premature preterm delivery and live birth. The patient lost her postpartum follow-up with no information available on the status of her ovaries.

Discussion

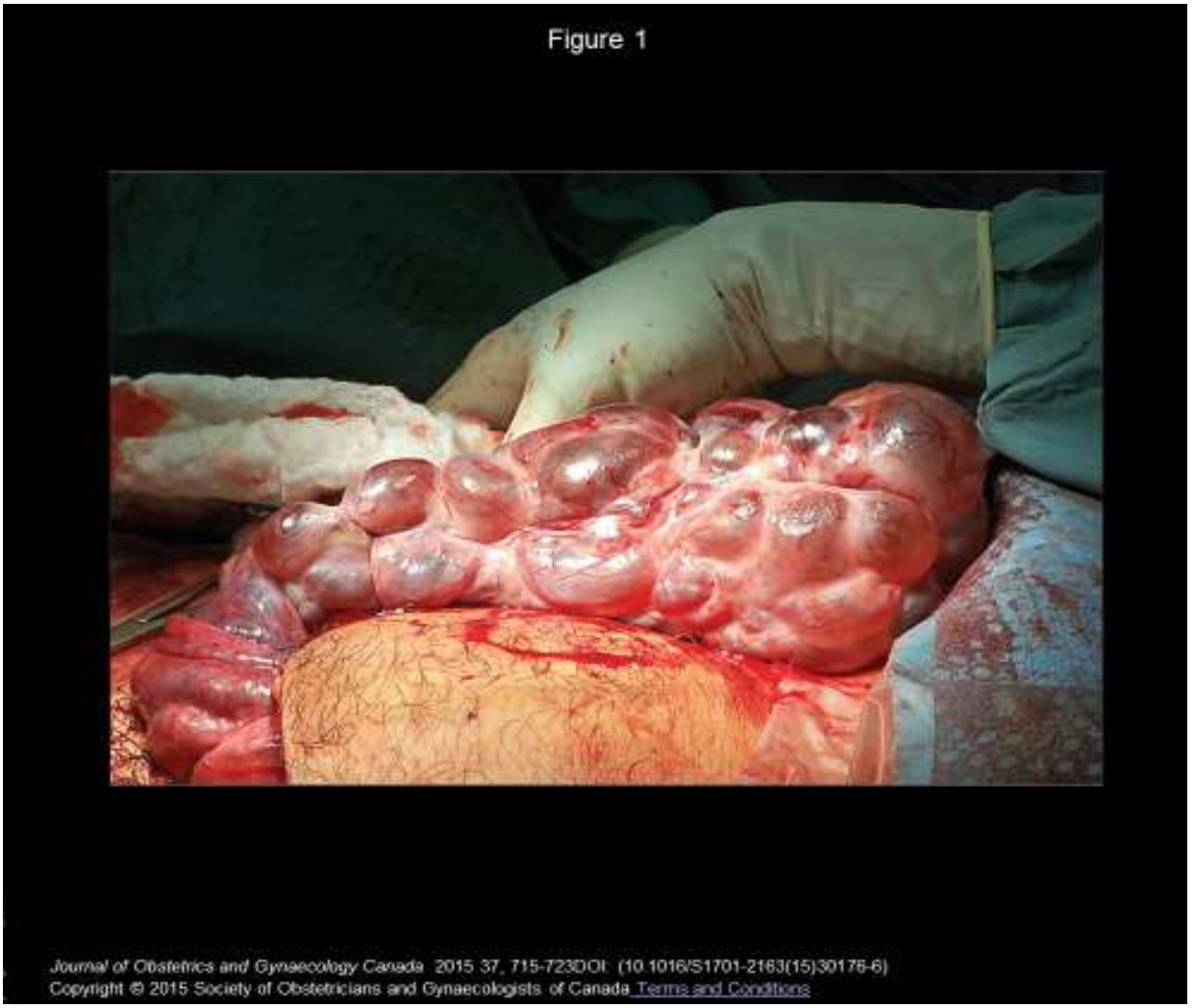
Hyperreactio Luteinalis (HL) is a condition caused by an overproduction of human chorionic gonadotrophin (HCG), a glycoprotein hormone. This condition is characterized by a young age, PCOS, lean body weight, high amh, high dose of Gonadotropins, elevated estradiol (E2), previous history of OHSS, and extremely high hCG levels. The condition is also known as Hyperreactio Luteinalis (HL) and is characterized by multiple pregnancy, multiple ovaries, ascites, and other physical findings suggestive of intravascular depletion. The HL is triggered by the overproduction of VEGF by follicles, leading to peritoneal neovascularization and vascular leak syndrome. This systemic impairment can lead to adverse events such as acute respiratory failure (ARDS) and hypovolemic shock.



Pathophysiology of OHS

Gonadotropin receptor mutations increase sensitivity to β-hCG, leading to the development of ca lutein cysts. HCG lacking the C-terminal peptide in the β-subunit has 10 times more potency than lh, causing ovarian stimulation. The degree of glycosylation affects gonadotropins' biological activity, with glycosylated variants

having increased activity. Hyperglycosylated HCG variants are also reported in hyperemesis gravidarum and trophoblastic diseases. This rare condition occurs in the first, second, or third trimester of pregnancy, multiple gestations, molar pregnancy, and in association with choriocarcinoma and fetal hydrops.



With their large number of locules, sohss may mimic a malignancy, in particular a mucinous borderline tumor of the intestinal type, and lead to unnecessary surgery (Van Holsbeke, et al.)

Us: s-ohss/ HL is characterized by large bilateral adnexal masses, many thin-walled small theca lutein cysts, classic appearance of a 'spoke wheel', and Ascites can be present. Lack of solid components help to differentiate sohss from ovarian malignancies.

A 2015 review by Malinowski et al. reported 58 pregnancies with HL, with 81% being singleton and 66.7% occurring in primiparous women. Comorbidities included hypothyroidism and gestational diabetes in 8.6% and 5.2%, respectively. Preterm delivery occurred in 28.9% of singleton pregnancies, preeclampsia in 19%, and intrauterine growth restriction in 31.7%. The study concluded a possible relationship between complications and increased B-hCG levels in pregnant patients with HL.

The classification of HL is useful but deficient, not encompassing Gonadotropin-secreting Pituitary Ademonas and trophoblastic diseases. Clinical manifestations include multicystic ovarian enlargement and elevated E2 levels. Pituitary adenoma does not cause pleural effusion and retention of ascites. Fluid sequestration in the third space was suggested for distinguishing between OHSS and ovarian hyperstimulation by a pituitary adenoma.

A 30-year-old patient required termination of pregnancy due to massive thrombophlebitis and severe ohss. After D&C, ascites resolved, possibly due to the absence of hCG and suppression of LH. Persistent large ovarian cysts were managed by oophorocystectomy before diagnosis of functional Gonadotropic Adenoma.

Approach to management

Historically surgical intervention was much more common in cases reported in earlier years the majority of reported cases in past few years have been successfully managed conservatively

Malinowski et al, found 36.2% have undergone surgery, of whom 23.8% had an acute complication (i.e., ovarian torsion, pain, hemoperitoneum) and the remaining 76.2% were suspected of having a malignancy.

tailored to the degree of severity

Early recognition, appropriate investigations/intervention/ treatment and close monitoring of condition is paramount to mitigating serious sequel.

Conclusion

Patients with bilateral mulitcystic ovaries, ascitis, and abnormally elevated B-hCG should be diagnosed with HL/S-OHSS in the first or early second trimester of pregnancy, even the absence of history of ovarian stimulation. Conservative management, with or without fluid tapping, is crucial to minimize iatrogenic harm. Close monitoring with ultrasound examinations is recommended to ensure normal ovarian architecture. Surgical intervention should be reserved for acute complications like cyst rupture, ovarian torsion, and haemorrhage to minimize unnecessary surgical and reproductive morbidity.

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