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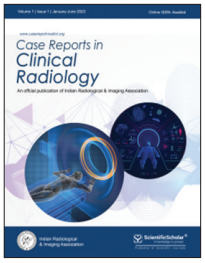

Case Report

Delving into an uncommon etiology of Mammoth ovaries

Rupa Renganathan[1], Divya Vishwanatha Kini[1], Prema Subramaniam[1], Shankar Dhandapani[2]

[1]Division of Breast and Women's Imaging and Interventions, Department of Diagnostic and Interventional Radiology, [2]Department of Endocrinology, Kovai Medical Center and Hospital, Coimbatore, Tamil Nadu, India.

***Corresponding author:**
Rupa Renganathan,
Division of Breast and Women's Imaging and Interventions, Department of Diagnostic and Interventional Radiology, Kovai Medical Center and Hospital, Coimbatore, Tamil Nadu, India.

drrrupa@gmail.com

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ABSTRACT

Ovarian hyperstimulation syndrome (OHSS) is an unusual clinico-radiological entity with a risk of developing life-threatening complications which have various etiologies. Radiological imaging helps image the typical features of enlarged ovaries and also helps rule out associated complications. Based on the severity of the clinical manifestations and corresponding radiological findings, grading systems have been devised as well. In this case report, we wish to highlight the features of this rare entity, that is, spontaneous OHSS, secondary to primary hypothyroidism in a young female who presented with acute abdomen.

Keywords: Enlarged ovaries, Ovarian hyperstimulation syndrome, Primary hypothyroidism, Ultrasound, Multiple cysts

INTRODUCTION

Ovarian hyperstimulation syndrome (OHSS) is an unusual clinico-radiological entity with a risk of developing life-threatening complications. It is primarily characterized by enlarged multicystic ovaries secondary to stimulation by various iatrogenic and non-iatrogenic triggers. Radiological imaging with various available modalities helps in assessing the primary pathology, its severity, and morphology in addition to ruling out other etiologies. In this case report, we wish to highlight the features of this rare entity, that is, spontaneous OHSS, secondary to primary hypothyroidism in a young female presenting with acute abdomen.

CASE REPORT

A 19-year-old female presented to our outpatient department with complaints of severe abdominal pain and non-projectile vomiting for the past 2 days. Her menstrual cycles were regular. On examination, she was found to have tenderness in the lower abdomen with no obvious mass that was palpable. Systemic examination was otherwise unremarkable and vitals were stable. Following this, in view of the abdominal pain, she was advised to have an ultrasound of the abdomen and pelvis. Ultrasound abdomen and pelvis (performed using GE Voluson E8, USA) demonstrated enlarged bilateral ovaries with multiple unilocular cysts within; no ascites, pleural effusion, or pericardial effusion was seen (the right ovary measured 157 cc and left ovary measured 202 cc) [Figure 1a and b]. Based on the ultrasound findings, a provisional diagnosis of OHSS was made. Corroborative magnetic resonance imaging (MRI) (3.0 T MRI, Siemens Healthineers, Germany) limited sections

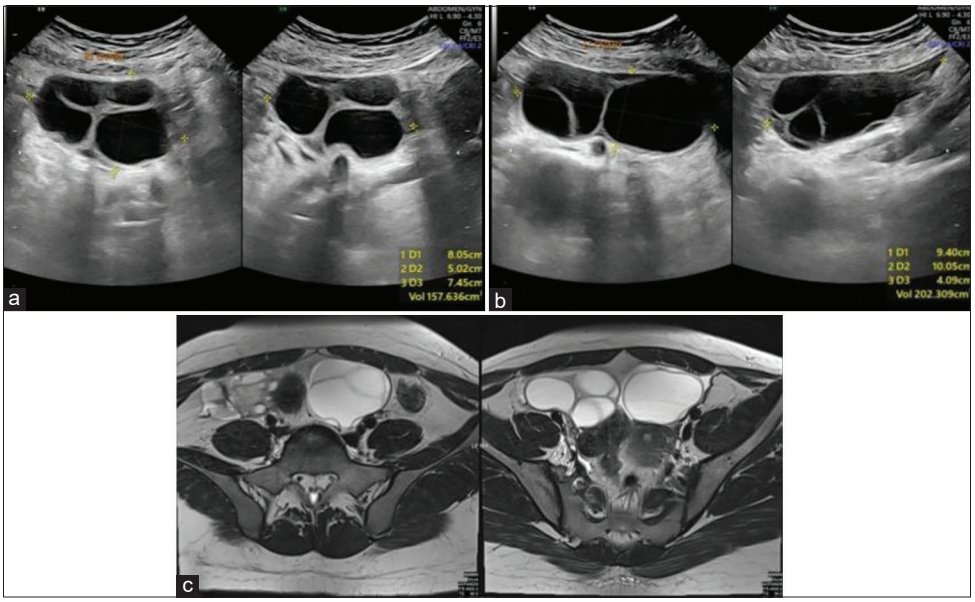

Figure 1: A 19-year-old female presented with ovarian hyperstimulation syndrome who presented with severe abdominal pain (a and b) ultrasound images showing bulky bilateral ovaries with multiple enlarged follicles and (c) axial T2-weighted magnetic resonance imaging section of the pelvis re-demonstrating the ultrasound findings of bulky ovaries with multiple follicles. No e/o torsion was noted.

of the pelvis were performed to rule out ovarian torsion and it depicted and confirmed the ultrasound findings of OHSS with no features of ovarian torsion [Figure 1c]. A provisional diagnosis of spontaneous ovarian hyperstimulation was made and a blood work-up was sent for further detailed analysis. Detailed scrutiny of the patient's history was done and possible etiologies such as pregnancy and iatrogenic causes such as ovarian stimulant drugs and hormone supplement intake were eliminated. Complete blood counts disclosed no significant abnormality; however, serum hormone level analysis revealed elevated serum estradiol (198.8 pg/mL, normal values 2.5–166 pg/mL), prolactin (121 ng/mL, normal values 0–30 ng/mL), and thyroid-stimulating hormone (TSH) (100 μU/mL, normal values 0.27–4.2 μU/mL) with a severely reduced free thyroxine levels (0.153 ng/dL). Beta-human chorionic gonadotropin (βHCG) levels were also assessed and found to be normal (<0.100 MIU/mL). A diagnosis of spontaneous OHSS secondary to primary hypothyroidism was made on assessment of the serum hormone levels in combination with the sonographic findings. Following this, the patient was then advised of thyroxine supplements (Tab THYRONORM 100 mcg) and was placed on regular follow-up with serial serum TSH level assessment and ultrasound abdomen to assess the ovarian volume. Clinical examination of her thyroid gland revealed diffusely enlarged gland with no obvious nodularity. The TSH levels exhibited a decreasing trend with the last recorded TSH level at 1 year follow-up being 3.44 μU/mL. The ovarian volumes were noted to reduce serially with volumes of 18 cc (right ovary) and 9 cc (left ovary) documented on the 5-month follow-up scan [Figure 2a-d].

DISCUSSION

The pathogenesis of OHSS is less-understood and a wide range of hypotheses exist, of which the most accepted is that of the role of glycoprotein hormones as a causative factor in genesis of spontaneous OHSS.[1] Glycoproteins such as serotonin, histamine, and prostaglandins influence the functioning of various existent mediators and vasoactive substances resulting in increased vascular permeability. This subsequently leads to the varied complications of OHSS such as deep vein thrombosis, ascites, pleural effusion, and hypercoagulability. In severe cases, organ dysfunction has also been noted.[2]

Multiple triggers have been noted to be associated with the occurrence of OHSS which may be classified as iatrogenic and non-iatrogenic causes.[1] Most common iatrogenic causes are secondary to ovulation therapy utilized for assisted reproductive techniques while some of the causes for non-iatrogenic causes resulting in spontaneous OHSS are pregnancy-related complications, gestational trophoblastic tumors, pituitary adenomas, and hypothyroidism.[3,4]

The association of OHSS with primary hypothyroidism has been noted in a few cases, such as in the report by Alzebidi *et al*. Although the pathogenesis of OHSS and its association with hypothyroidism is unclear, few theories in relation to modifications in the hydroxylation pathway and feedback regulation have been noted.[5]

Role of imaging in OHSS is vital with the availability of rapid and accurate modalities such as ultrasonography to make the diagnosis and also to detect its complications.[1] The

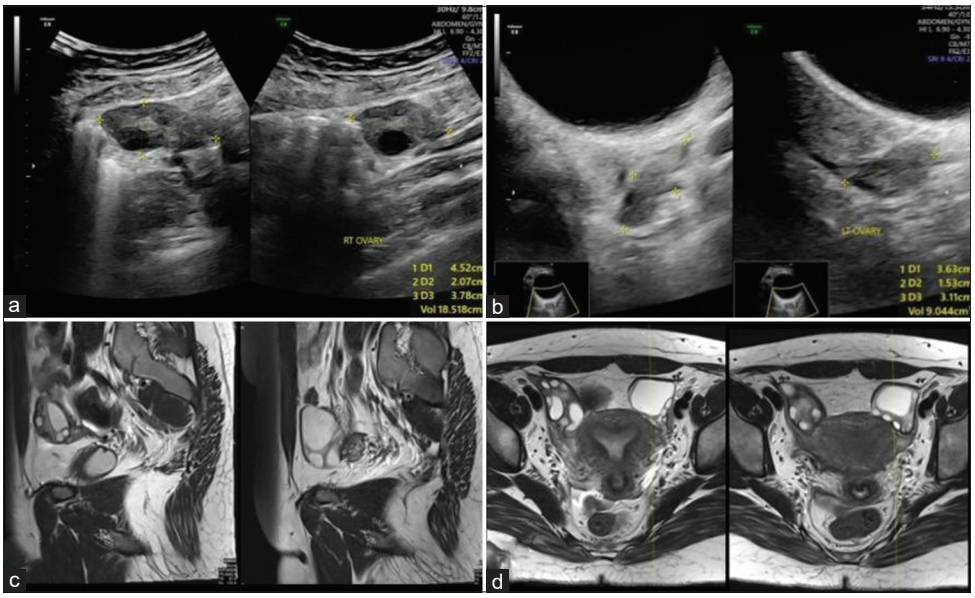

Figure 2: A 19-year-old female presented with ovarian hyperstimulation syndrome (OHSS) who had presented with severe abdominal pain, diagnosed as OHSS, on follow-up (a and b) Ultrasound images demonstrating the normal size and morphology of both ovaries at 5 month follow-up (c and d) sagittal and axial T2-weighted magnetic resonance imaging section of the pelvis re-demonstrating ultrasound findings suggesting complete resolution.

Table 1: Golan grading system of OHSS.

Category	Grade	Clinical Features
Mild OHSS	Grade 1	Abdominal distention and discomfort
	Grade 2	Grade 1+Vomiting, Nausea+Ovarian size of 5–12 cm
Moderate OHSS	Grade 3	Mild OHSS+Ascites
Severe OHSS	Grade 4	Moderate OHSS+Pleural/Pericardial effusion
	Grade 5	Grade 4+Biochemical imbalance

OHSS: Ovarian hyperstimulation syndrome

Table 2: Modified Deleneers classification of OHSS.

Modified Deleneers classification	Pathology	Trigger
I	Mutated FSHR	Pregnancy
II	Elevated β-HCG	Multiple pregnancies Gestational trophoblastic disorders βHCG secreting tumors
III	Elevated TSH	Hypothyroidism
IV	Elevated FSH/LH	FSH/LH secreting pituitary adenomas Ectopic FSH secreting tumors

OHSS: Ovarian hyperstimulation syndrome; FSHR: Follicle-stimulating hormone receptor; βHCG: Beta-human chorionic gonadotropin, TSH: Thyroid-stimulating hormone; FSH: Follicle-stimulating hormone; LH: Luteinizing Hormone

typical imaging feature is that of enlarged bilateral ovaries with multiple cysts of varying sizes within. The cysts may be secondarily complicated with hemorrhage; however, the presence of solid components or vascularity within the cysts is not seen. In addition, other features such as ascites, pleural effusion, pericardial effusion, and deep vein thrombosis can also be efficiently detected.[1]

Based on the severity of the clinical manifestations and corresponding radiological findings, a grading system has been devised by Golan to categorize OHSS into mild, moderate, and severe [Table 1].[1,6,7] However, based on the etiology of OHSS, the modified Deleneers classification is widely used which was modified by Panagiotopoulou *et al.* based on the presence of follicle-stimulating hormone receptor (FSHR) mutation and levels of βHCG, TSH, follicle-stimulating hormone, and luteinizing hormone levels [Table 2].[8,9]

An important and clinically similar entity that is imperative to be ruled out is the possibility of ovarian torsion – isolated or superadded. This is a possible complication as well as a close differential and use of ultrasound, an easily accessible tool, helps decipher this. Ovarian torsion in association with OHSS is found to be more commonly seen in pregnancy with an incidence of up to 16%.[10]

OHSS, due to its rarity, is a less understood concept in the medical literature. Moreover, with the increasing number of individuals utilizing assisted reproductive techniques in

the present day, its incidence has been noted to be in higher numbers. However, the possibility of the existence of this pathology even in cases not presenting with a typical clinical history is to be made aware to clinicians and radiologists alike as only then will a search for other possible etiologies be made. To conclude, acquiring a detailed history and corroborating it with appropriate imaging techniques and confirmatory hormonal analysis is a necessary prerequisite to any case presenting with suspected OHSS. Thus, the prompt diagnosis of the same by a radiologist is vital in planning early intervention thereby delivering efficient patient care.

DIFFERENTIAL DIAGNOSIS

Although comprising typical imaging features, when cases are of the milder variety few possible differentials [Table 3]:

Table 3: Differential diagnosis of ovarian hyperstimulation syndrome.

Polycystic ovaries	• The cysts are usually smaller in size with a relatively smaller ovarian volume • History of menstrual cycle irregularity and hirsuitism • Not associated with fluid accumulation such as ascites and pleural effusion • No history of clinical presentation with acute abdomen/associated etiological triggers
Ovarian torsion	• Presents with an acute abdomen and the clinical presentation may overlap • It may even coexist secondary to OHSS • Imaging features of a unilateral enlarged ovary with peripherally displaced follicles and central edematous stroma is noted. However, features of third space fluid loss (pleural effusion, ascites), as in OHSS, are not typically seen
Theca lutein cysts associated with GTT	• It may be an associated component with OHSS. • Typical imaging features of trophoblastic proliferation are noted in GTT within the uterus on USG/MRI points to this as the etiology. • Grossly elevated β-HCG with history of hyperemesis and/or hypertension is seen
Mucinous ovarian neoplasm	• Usually multiloculated bilateral adnexal pathology with typically varying signal intensity contents within • When malignant, they are larger with associated solid components and metastatic deposits • They are unlikely to present as an acute abdomen

GTT: Gestational trophoblastic disease, OHSS: Ovarian hyperstimulation syndrome, USG: Ultrasound, MRI: Magnetic resonance imaging, β-HCG: Beta human chorionic gonadotropin

CONCLUSION

Ovarian hyperstimulation syndrome is an entity comprising typical imaging features that warrant an immediate spot diagnosis. Also, as a clinical radiologist, familiarising ourselves with remote causes helps us make a complete diagnosis.

TEACHING POINTS

1. Enlarged ovaries with multiple cysts are a typical imaging feature of OHSS and should guide a prompt diagnosis from the radiologist. It should also direct them to obtain a detailed history pertaining to the etiological triggers for OHSS.
2. Thorough assessment of the patient for possible complications related to OHSS such as extravascular fluid accumulation, hypercoagulability, and thromboembolism.

MCQs

1. OHSS is not associated with
   a. Gestational trophoblastic tumors
   b. Pituitary adenomas
   c. Hypothyroidism
   d. Diabetes mellitus

Answer key: d

2. Differential for OHSS is
   a. Polycystic ovaries
   b. Theca lutein cysts associated with GTT
   c. Mucinous ovarian tumors
   d. All the above

Answer key: d

3. Following are the criteria for staging of OHSS
   a. Golan
   b. Modified Deleneers
   c. a and b
   d. None of the above

Answer key: c

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the

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