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A case of spontaneous ovarian hyperstimulation syndrome (SOHSS) due to hypothyroidism

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CASE STUDY

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ABSTRACT

A 15-year-old girl who was previously diagnosed to have primary hypothyroidism presented to the outpatient department in our tertiary care centre in Southern India with abdominal distension and pedal oedema. On evaluation, she was found to have elevated lactate dehydrogenase (LDH) and CA 125 levels, enlarged multicystic ovaries, ascites, and pleural and pericardial effusions. A diagnosis of spontaneous ovarian hyperstimulation syndrome (SOHSS) was made based on the characteristic soap bubble-like imaging appearance of ovaries in the background of hypothyroidism and she was started on thyroxine. At her three-month follow-up, the patient's biochemical parameters normalised with reduced ovarian volume and resolution of other imaging findings. SOHSS needs to be considered in patients with hypothyroidism and characteristic multicystic ovarian enlargement.

Key Words
Hypothyroidism, spontaneous ovarian hyperstimulation syndrome, multicystic ovaries, soap bubble appearance

Implications for Practice:

1. What is known about this subject?
Hypothyroidism is a very rare cause of spontaneous ovarian hyperstimulation syndrome (SOHSS). These patients present with multicystic ovaries, which can be mistaken for ovarian malignancy.

2. What new information is offered in this case study?
This case study emphasises the need to consider the diagnosis of SOHSS at initial presentation when there are typical imaging findings in the background of hypothyroidism, and to initiate thyroxine supplementation promptly without opting for surgery or further unwarranted investigations.

3. What are the implications for research, policy, or practice?
SOHSS caused by hypothyroidism is completely reversible with thyroxine supplementation. Knowledge of this rare condition is necessary as misdiagnosis can lead to unwarranted surgery.

Background

Ovarian hyperstimulation syndrome (OHSS) is a well described and commonly known condition seen in patients undergoing treatment for infertility. Its rarer counterpart, spontaneous ovarian hyperstimulation syndrome (SOHSS) is a less known condition that occurs in the absence of any external hormonal stimulation and is associated with conditions causing a high level of serum human chorionic gonadotropin (hCG) such as multifetal pregnancy, gestational trophoblastic disease,[1–4] and polycystic ovarian disease. Other less common causes for SOHSS include singleton pregnancy,[5] hypothyroidism,[6–8] and follicle-

stimulating hormone-producing (FSH-producing) pituitary adenoma.[9]

The clinical presentation is the same in both iatrogenic and spontaneous OHSS, however, the spontaneous variety is often misdiagnosed as malignancy because of poor awareness of this entity among gynaecologists, physicians, and radiologists. Often patients are pre-pubertal or adolescent girls who present with enlarged multicystic ovaries, ascites, pleural effusion, and may even have elevated CA 125 levels leading the clinician to make a diagnosis of ovarian malignancy[6,10,11] and thereby subjecting patients to unwarranted surgery. In this case study, we describe the typical imaging findings that can help identify the benignity of this condition and therefore avoid unnecessary surgical morbidity.

Case details

A 15-year-old girl presented to the outpatient department of our tertiary care centre in Southern India with decreased appetite for one month, abdominal distension, and pedal oedema for two weeks. There was no history of weight loss. She also had irregular menstrual cycles since she attained menarche at 13 years of age. She was diagnosed to have hypothyroidism at nine years of age, for which she was on thyroxine supplementation for two years. Subsequently, she stopped the medication for no definite reason. She was otherwise asymptomatic until one month before.

On examination, she was of small build (body mass index=18.2kg/m^2), had pallor, and bilateral pitting pedal oedema. Her thyroid gland was not palpable. Abdominal examination revealed a lobulated mass in the lower abdomen extending till the level of the umbilicus. Lower border of the mass was not felt and the mass was extending into the pelvis. The rest of the systemic examination was unremarkable.

Investigations and Imaging

Laboratory investigations (normal range) revealed severe primary hypothyroidism (thyroid-stimulating hormone (TSH) 750micro IU/ml (0.3–4.5micro IU/ml); total thyroxine (T4) 8.5micro gm per cent (4.5–12.5micro gm per cent); free thyroxine 0.60nano gm per cent (0.8–2 nano gm per cent); elevated CA 125 level 98 U/l (<35U/l); elevated LDH level 657U/l (225–460U/l); normal beta-hCG level <0.100mIU/ml (<5.0mIU/ml); and normal alpha-fetoprotein (AFP) level 2.12IU/ml (<5.5IU/ml).

A CT scan of the abdomen (Figure 1) showed markedly enlarged multicystic ovaries with thin septations giving them a “soap bubble” appearance; mild ascites; mild pericardial effusion; and a bilateral thin sliver of pleural effusions. There was no evidence of peritoneal thickening or enhancing soft tissue deposits. There were no other abnormal findings.

Ultrasound of the neck (Figure 2) showed a diffusely enlarged thyroid gland with altered echotexture and a few anechoic cysts in both lobes; one of the larger cysts showed a thin septation within.

Diagnosis and follow-up

In the background of severe hypothyroidism, enlarged multicystic ovaries raised the possibility of SOHSS. The other differential diagnoses considered were as follows: epithelial origin-cystic ovarian neoplasm in view of the mildly elevated CA 125 level; and dysgerminoma in view of the raised LDH level. However, the typical soap bubble appearance of enlarged ovaries along with lack of peritoneal and omental tumour deposits in the background of untreated hypothyroidism made the diagnosis of SOHSS most likely. Hence, it was decided to treat the hypothyroidism with oral thyroxine supplementation and follow up with the patient.

At her three-month follow-up, there was complete resolution of abdominal distension and pedal oedema with regularisation of menstrual cycles. There was also normalisation of serum TSH (2.52micro IU/ml) and CA 125 (8.32U/l) levels. A repeat CT scan of the abdomen (Figure 3) showed marked reduction in ovarian volume with resolution of pleural and pericardial effusions, and ascites, thereby confirming the diagnosis of SOHSS. Ultrasound of the neck (Figure 4) showed complete resolution of the cysts in the thyroid gland.

Discussion

SOHSS is a less common subtype of OHSS that occurs in the absence of any iatrogenic hormonal stimulation. Clinical manifestations of OHSS include abdominal distension, ascites, pleural effusion, oliguria, electrolyte imbalance, and hemoconcentration[6] due to acute fluid shift from intravascular space into the extravascular space. Hemodilution has been reported in a case of SOHSS following natural conception.[11]

The exact mechanism by which hypothyroidism causes ovarian hyperstimulation is unclear. Possible mechanisms include: (1) TSH-mediated stimulation of FSH receptor[8–10,12]

often associated with FSH receptor mutation; (2) increased TRH production in hypothyroidism resulting in GnRH receptor activation[8]; and (3) preferential formation of estriol in patients with hypothyroidism, which is a weaker suppressor of gonadotropin release than estradiol.[6] Vasoactive peptides released by the granulosa cells in hyperstimulated ovaries result in an increase in vascular permeability causing a shift of fluid from intravascular compartment to the extravascular compartment/third space resulting in hypovolemia with concomitant ascites, pleural effusion, and oedema.

Radiological findings in OHSS (both spontaneous and iatrogenic types) include enlarged multicystic ovaries with ascites, and pleural and pericardial effusions. The typical radiological finding that helps in making the correct diagnosis of OHSS is the wheel spoke or soap bubble appearance of the enlarged ovaries resulting from multiple enlarged follicles arranged peripherally around a central stroma. The “spokes” of the wheel or the “pseudo-septa” result from normal stroma that is compressed between the enlarged follicles. To the best of our knowledge, this finding has been reported in only two cases of spontaneous OHSS caused by hypothyroidism in the published literature.[6,13]

This ovarian morphology, which can be demonstrated on trans-abdominal ultrasound, CT, or MRI is a pointer towards benignity and one should be cautious about labelling ovarian cysts with these features as ovarian malignancy. A literature search revealed that most case reports of hypothyroidism resulting in SOHSS[7,8,10,11,14–17] simply mention the enlarged multicystic ovaries, but had not commented on typical imaging appearance of ovaries that would help us differentiate this condition from malignancy with reasonable certainity. Many of these case reports[8,14,16,17] also state that malignancy was considered as the initial working diagnosis and work-up was done for the same before a final diagnosis of SOHSS had been established. In one case report, the patient had undergone laparoscopic biopsy of the ovaries before correct diagnosis could be made.[8]

In another article, the authors mentioned that the patient underwent unilateral oophorectomy and contralateral ovarian cystectomy before the diagnosis of SOHSS was made; the patient eventually developed infertility due to poor ovarian reserve.[10] In this article, we emphasise the importance of identifying this imaging finding in all patients with enlarged multicystic ovaries. However, we do not recommend universal screening of thyroid function in all patients with multicystic ovaries in view of the rarity of SOHSS. Instead, screening for hypothyroidism may be reserved for such cases where clinical features of hypothyroidism are present or, alternatively, when the imaging findings point towards benignity.

There is resolution of the cystic ovarian enlargement and fluid in the third-space compartments following appropriate treatment of the underlying cause, which is well demonstrated in our case within three months after initiation of thyroid hormone replacement therapy. Elevated CA 125 level has been documented in several non-malignant conditions, including hypothyroidism. In addition, all conditions that irritate serous membranes may also show elevated serum CA 125 level.[6]

Conclusion

Enlarged multicystic ovaries with pleural effusion, pericardial effusion, and ascites have been classically described in spontaneous ovarian hyperstimulation syndrome (SOHSS) associated with hypothyroidism. Although ovarian malignancy is a differential in such cases, the typical wheel spoke or soap bubble appearance of the enlarged ovaries on imaging is a useful tool in differentiating the benign nature of SOHSS from malignancy. Knowledge of this uncommon condition among gynaecologists, radiologists, and primary care physicians is essential to avoid misdiagnosis of this condition.

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PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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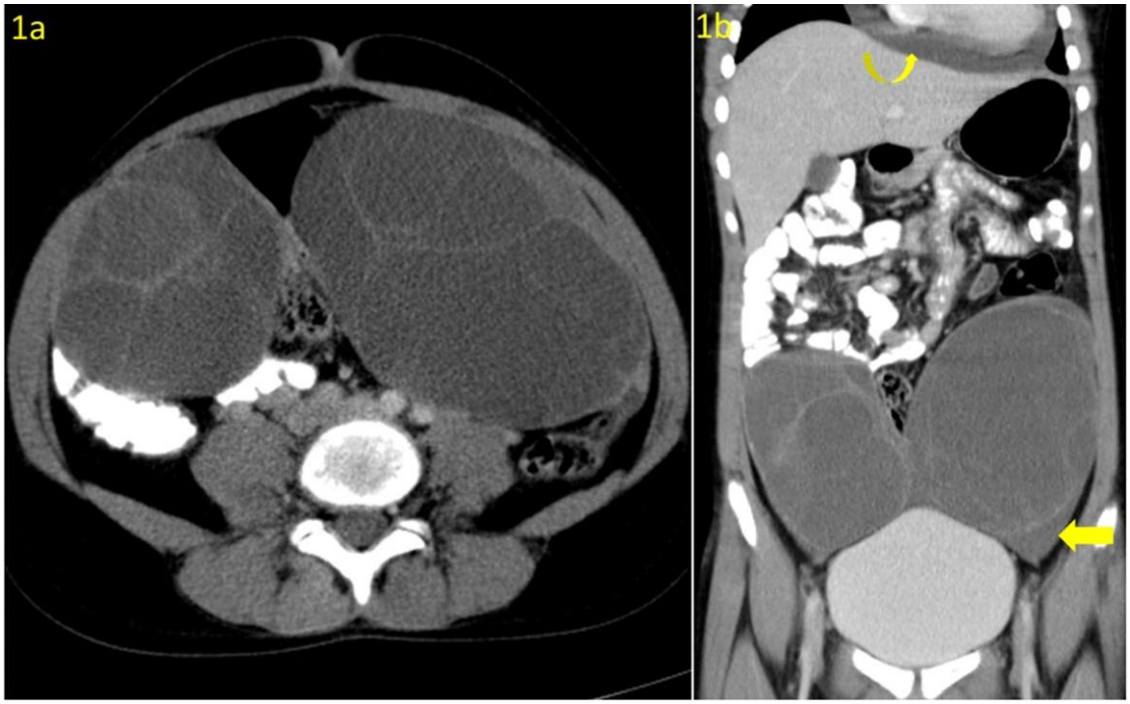
PATIENT CONSENT

The authors, *Putta T, John R, Thomas N, Jebasingh F, Peedicayil A, Eapen A*, declare that:

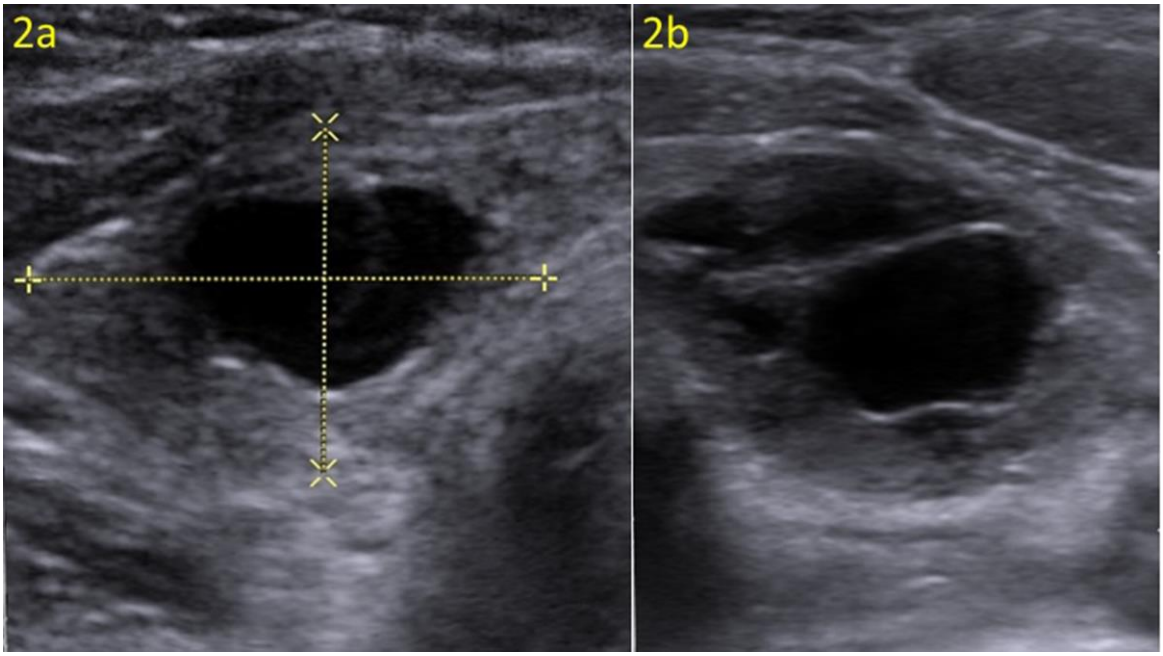
1. They have obtained written, informed consent for the publication of the details relating to the patient in this report.
2. All possible steps have been taken to safeguard the identity of the patient.
3. This submission is compliant with the requirements of local research ethics committees.

Figure 1: **CT showing bilateral enlarged multicystic ovaries**



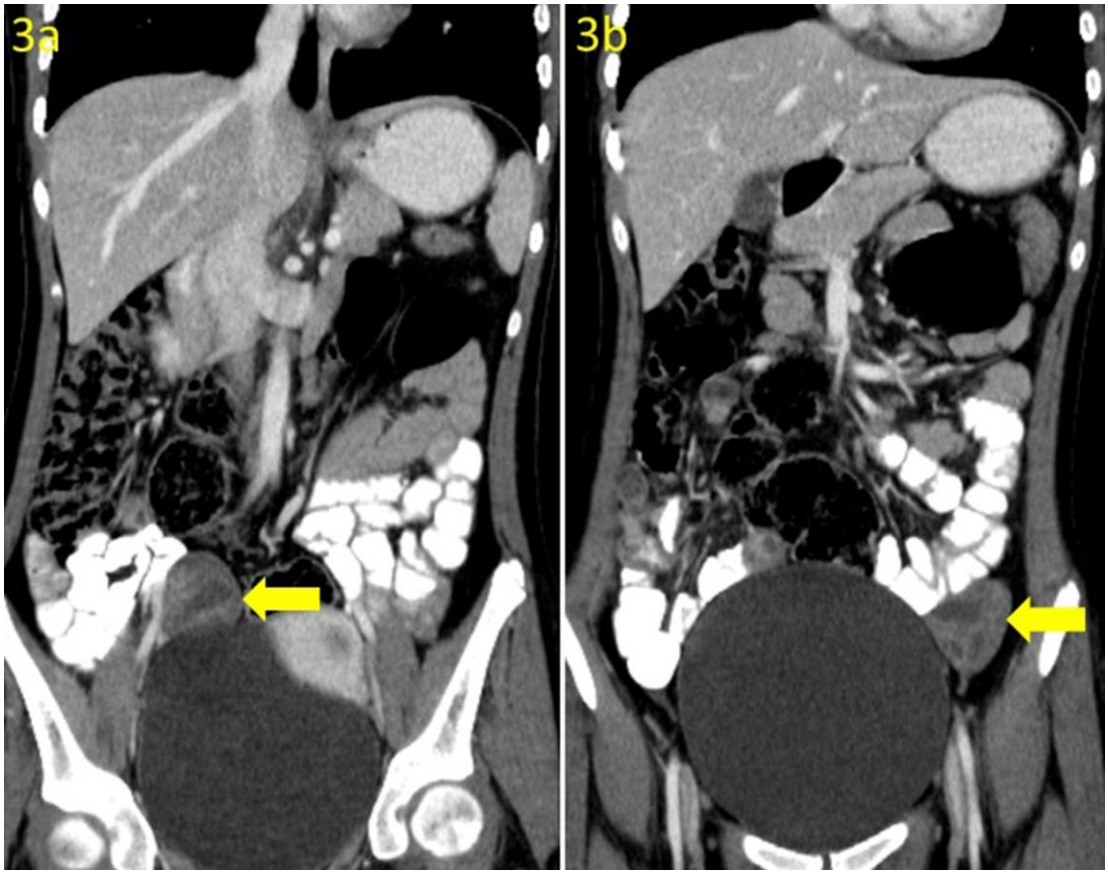
Representative axial (1a) and coronal (1b) sections of CT abdomen showing bilateral enlarged multicystic ovaries with a soap bubble appearance. Ascites (solid straight arrow) and pericardial effusion (curved arrow) are also evident on the coronal image.

Figure 2: **Ultrasound of thyroid gland**



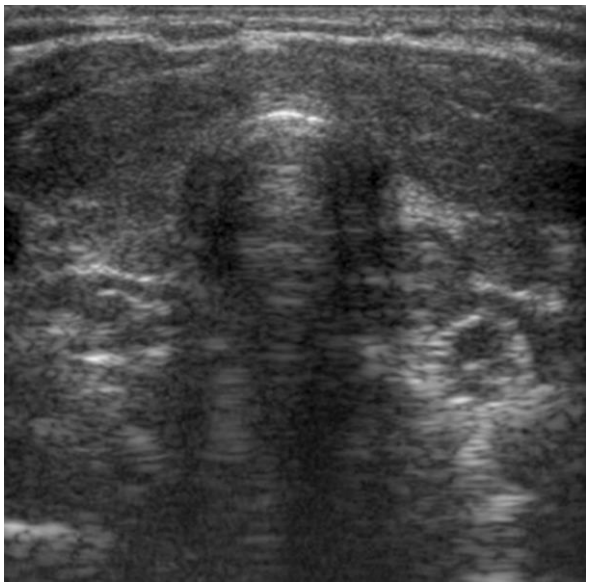
Ultrasound images of the thyroid gland (2a and 2b) showing altered echotexture with anechoic cysts within the gland.

Figure 3: **CT abdomen coronal images at three-month follow-up**



CT abdomen coronal images (3a and 3b) at three-month follow-up showing normal sized ovaries (solid straight arrows – right ovary in 3a and left ovary in 3b). There is resolution of the ascites and pericardial effusion that was seen on the initial CT.

Figure 4: **Ultrasound of thyroid gland at three-month follow-up**



Ultrasound of thyroid gland at three-month follow-up showing resolution of the thyroid cysts.