

Ovarian cyst regression with levothyroxine in ovarian hyperstimulation syndrome associated with hypothyroidism

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Summary

Background: Spontaneous ovarian hyperstimulation syndrome (sOHSS) can occur following hypothyroidism.

Ultrasonography facilitates diagnosis and monitoring of this syndrome. We describe ovarian sonographic changes in a hypothyroid patient with sOHSS after treatment with levothyroxine (L-T₄).

Case presentation: A 15-year-old girl presented with abdominal pain and distension for a few months. On examination, she had classical features of hypothyroidism. Abdominal and pelvic ultrasound revealed enlarged ovaries with multiple thin-walled cysts and mild ascitic fluid. On follow-up, abdominal ultrasound showed significant reduction of ovary size after 6 weeks of initiation of L-T₄. Normal ovary size with complete regression of ovarian cysts was seen after 4 months.

Conclusion: Serial ultrasound in sOHSS associated with hypothyroidism showed regression of ovarian cysts and ovarian volume after 4 months whereas in other studies, it is reported to happen in various durations, presumably according to its etiology.

Learning points:

- OHSS can rarely occur due to hypothyroidism.
- This type of OHSS can be simply treated by L-T₄ replacement, rather than conservative management or surgery in severe cases.
- Ultrasound follow-up shows significant regression of ovarian size and cysts within 6 weeks of initiation of L-T₄.
- Ultrasound follow-up shows normal ovarian size with complete resolution of ovarian cysts 4 months after treatment.

Background

Ovarian hyperstimulation syndrome (OHSS) is usually iatrogenic and is a potentially life-threatening complication of ovulation induction. Spontaneous OHSS might occur following high levels of human chorionic gonadotropin (HCG) in normal pregnancy, hypothyroidism, or FSH receptor mutation (1). Expanding use of

ultrasonography facilitates the diagnosis and monitoring of the treatment of this syndrome (2).

We have described this syndrome in a girl virgin with primary autoimmune hypothyroidism in our previous article (3); we followed her by serial abdominal ultrasound that showed normal ovary size and regression of ovarian cysts after levothyroxine (L-T₄) replacement.

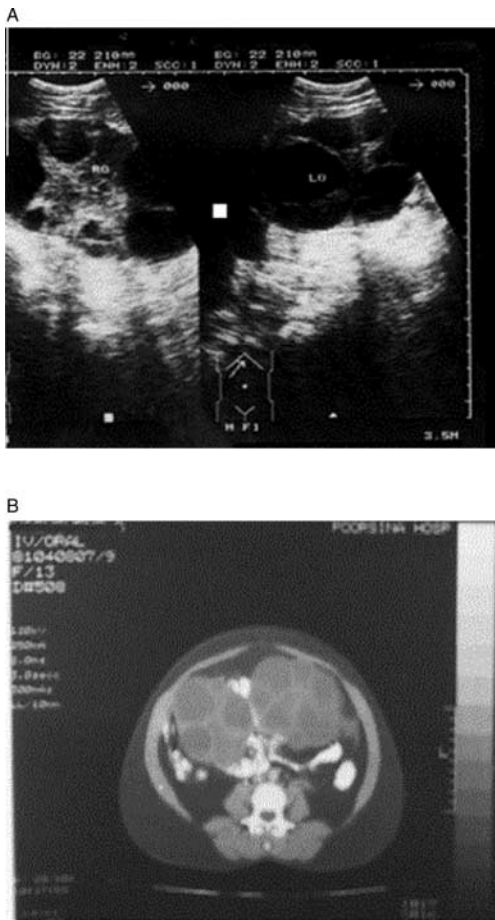


Figure 1
Imaging findings show bilateral multiloculated ovarian cysts.
(A) Abdominal ultrasound and (B) abdominal CT scan (3).

Case presentation

A 15-year-old girl presented with abdominal pain and distension for a few months. On examination, she had classical features of hypothyroidism (3). The abdomen was distended and non-tender with a large palpable mass in the lower abdomen extending to the upper abdomen.

Investigation

Laboratory findings included the following: Hb=11.2 g/dl, Hct=36.2%, MCV=81 fl, MCH=28.2 pg, BUN=13 mg/dl, Cr=0.7 mg/dl, cholesterol=290 mg/dl, and TG=273 mg/dl. Hormonal studies confirmed hypothyroidism: serum TSH >100 mIU/l, total T₄=1.8 µg/dl (normal: 4.4–12.5 µg/dl, radioimmunoassay (RIA)), T3RU=31.2% (normal: 25–34.4%), anti-TPO antibody=290 U/ml (normal <70, ELISA), and prolactin=176 ng/ml

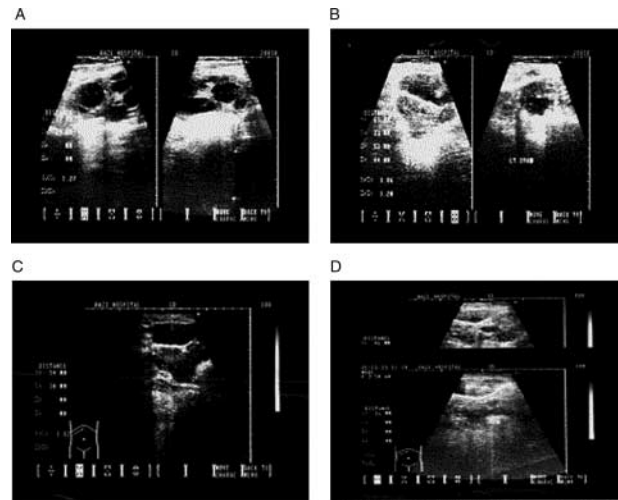


Figure 2
Follow-up abdominal sonography showed significant ovarian volume and cyst regression within 4 months of levothyroxine therapy (A) after 2 months, (B) after 4 months, (C) after 8 months (right ovary), and (D) after 8 months (left ovary).

(normal: 3–21, RIA) (3). Abdominal and pelvic ultrasound revealed enlarged ovaries that occupied the whole abdomen and pelvic cavity: right ovary, 150×75×62 mm with a volume of 454 cc; left ovary, 130×70×68 mm with a volume of 340 cc. It also represented multiple thin-walled cysts and mild ascitic fluid. Abdominal and pelvic

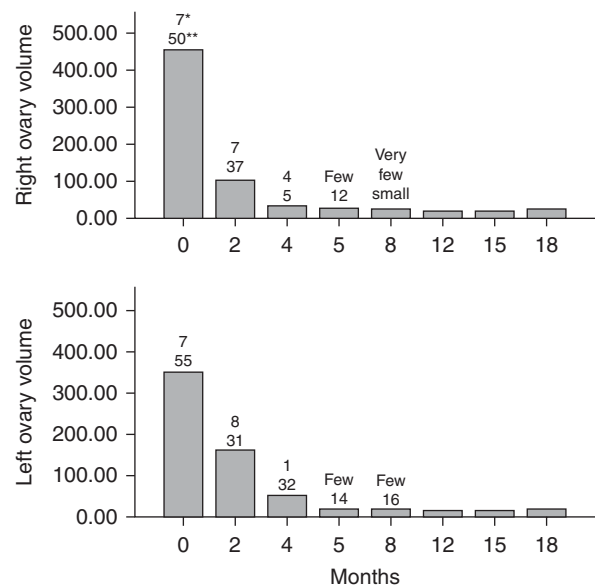


Figure 3
Right and left ovarian volume change after levothyroxine replacement.
*Upper digit shows the number of cysts and **lower digit shows the largest diameter of the largest cyst.



Table 1 Summary of case reports describing patients with OHSS associated with hypothyroidism.

Reference	Age (years)	Hypothyroidism	Pregnancy	FSH receptor mutation	Sonographic report	Treatment	Follow-up
Heydari et al. (3)	15	TSH > 100 mIU/l Ab:Neg.	-	Neg.	Enlarged ovaries with multiple ovarian cysts Rt: 150×75×62 Lt: 130×70×68 Multiple large cysts with rupture of one cyst Rt: 110×65 Lt: 118×58	Levothyroxine (100 µg)	After 4 months: normal ovary size and regression of cysts After 4 months: normal
Akbay et al. (13)	21 (P1)	TSH = 8.75 mIU/l Ab:NA	10 weeks HCG = NI	NA	Bilateral multilobulated cystic 130×80 sized ovaries	Levothyroxine (100 µg)	After 3 months of delivery: normal
	23 (P2)	TSH = 2.16 mIU/l Ab:NA	12 weeks HCG = NI		Bilateral multilobulated cysts Rt: 13×70 Lt: 110×70	Levothyroxine (100 µg)	After 2 months of delivery: normal
Dietrich et al. (15)	26 (P1)	Normal	12 weeks HCG = 118 665	Present (D567N)	Bilateral multicystic ovaries Rt: 140×150 Lt: 120×130	Conservative	Abortion at 15 weeks
	26 (P2)	TSH = 5.51 mIU/l Ab:NA	10 weeks HCG = 147 688		Enlarged ovaries Rt: 100×100 Lt: 100×100	Levothyroxine (100 µg)	Normal delivery at term
Lussiana et al. (16)	29	TSH = 5.92 mIU/l Ab:NA	22 weeks (with abortion)	Present (with undetermined significance)	Bilateral multiple ovarian cysts Rt: 200×110 Lt: 160×120	Levothyroxine	After 3 months of abortion: normal ovaries
Edwards et al. (9)	30	TSH = 41.7 mIU/l	10 weeks HCG = 291 206	NA	Enlarged mass	Levothyroxine	By 22 weeks of gestation: ovarian regression 10 weeks after delivery: normal ovaries
Borna et al. (12)	30	TSH > 400 mIU/l Ab:NA	20 weeks HCG = NI	NA	Bilateral multilobulated ovarian cysts Rt: 200×160 Lt: 160×100	Levothyroxine (200 µg)	After 3 months: resolution of cysts After 6 months: normal ovary size
Sultan et al. (11)	12	TSH = 1310 mIU/l Ab:Neg.	-	Neg.	Large cystic structure	Levothyroxine	
Mousavi et al. (6)	26	TSH > 50 mIU/l Ab:NA	-	NA	Bilateral multiseptated ovarian masses Rt: 69×63×96 Lt: 66×63×99	Levothyroxine (100 µg)	



Table 1 Continued

Reference	Age (years)	Hypothyroidism	Pregnancy	FSH receptor mutation	Sonographic report	Treatment	Follow-up
Taher <i>et al.</i> (10)	22	TSH > 100 mIU/l Ab:NA	-	NA	Bilateral multilobulated ovarian mass with cystic component Rt: 90 × 120 Lt: 60 × 40	Levothyroxine (100 µg)	After 3 months: marked reduction
Corsado <i>et al.</i> (7)	25	TSH = 210 mIU/l Ab:Neg.	11 weeks HCG = 15 890	NA	Bilateral multilobulated ovarian cysts Rt: 160 × 150 Lt: 160 × 130	Levothyroxine (100 µg)	By 24 weeks of gestation: normal ovary

Ab, antithyroglobulin/anti-peroxidase antibody; Neg, negative; NA, not available; P, pregnancy; HCG, human chorionic gonadotropin (IU/l); NI, normal (according to gestational age); Rt and Lt, right and left ovaries (mm²).

computed tomography (CT) scan showed these thin-walled cysts with no enhancement.

Treatment

She was started on L-T₄ 100 µg/day.

Outcome and follow-up

On follow-up ultrasound, the size of the ovaries became significantly smaller 6 weeks after L-T₄ replacement and became normal with complete resolution of cysts after 4 months (Figs 1 and 2).

Discussion

A description of OHSS in two members of a family has recently been published (3), but there are a few studies focusing on ovarian volume and cyst regression after L-T₄ replacement therapy. Imaging findings in OHSS include multiple, large, and thin-walled cysts and ascitic fluid in severe forms (4). The exclusion of diagnosis of ovarian cancer is made by ultrasonography and CT scan or magnetic resonance imaging (MRI), which reveals the classical 'spoke wheel' appearance that is characteristic of theca lutein cysts without solid components. Furthermore, the reduction in ovarian volume and regression of detected cysts during close observational management and ultrasonic follow-up can differentiate OHSS from other diagnoses (5).

Here, we described resolution of ovarian cysts and normalization of the size of the ovaries in our patient 4 months after L-T₄ administration (Fig. 3). It is noteworthy that the kinetics of the symptoms are closely related to the life span of corpus luteum. In the absence of pregnancy, symptoms resolve spontaneously with the onset of menses, while in the presence of pregnancy, symptoms start to improve after the sixth week of pregnancy, before HCG peak (1). However, in OHSS with underlying disease such as hypothyroidism, complicated pregnancies or in the presence of mutated FSH receptor genes, the symptoms have been reported to last longer (6) (7) (8) (9) (10) (11) (12) (13) (14). Mousavi *et al.* (6) reported normalization of ovarian appearance in ultrasound 6 months after L-T₄ replacement therapy. In other studies on hypothyroid patients (with and without pregnancy), considerable regression of cysts was observed after 3 months (7) (8) (9) (10) (11), with an exception that in three case reports patients experienced total regression 3 months after delivery (12) (13) (14) (Table 1). Rising serum level of

endogenous HCG might strengthen the severity of OHSS in pregnant patients and would lead to a more complicated course than patients with hypothyroidism (15).

In conclusion, ultrasonography as well as CT scan or MRI assists the diagnosis of OHSS. By serial ultrasound, we observed regression of ovarian cysts and ovarian volume after 4 months whereas in other studies, it is reported to happen in various durations that may be related to the etiology of this syndrome.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Funding

This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

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Received in final form 6 May 2013

Accepted 15 May 2013