CASE REPORT

CYPRUS
JOURNAL OF MEDICAL SCIENCES

DOI: 10.4274/cjms.2024.2024-58
Cyprus J Med Sci 2024;9(6):450-453

A Case of Primary Hypothyroidism Complicated with Pituitary Pseudo-Macroadenoma and Chronic Adnexal Torsion

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Abstract

Primary hypothyroidism with extremely high thyroid-stimulating hormone levels can cause bilateral theca lutein cysts and pituitary pseudo-macroadenoma. We report a case of bilateral ovarian cysts complicated by chronic adnexal torsion. Although the size of the pituitary pseudo-macroadenoma and the right ovary decreased after successful levothyroxine treatment, it was determined that the opposite ovary was torsioned. We suggest that ovarian hyperstimulation due to severe primary hypothyroidism can be treated medically and that possible complications should be closely monitored.

Keywords: Chronic ovarian torsion, pituitary pseudo-macroadenoma, primary hypothyroidism, theca lutein cysts

INTRODUCTION

Hypothyroidism is a serious metabolic disorder with multisystem effects. Ovarian cyst formation mimicking ovarian hyperstimulation syndrome is a rare complication of untreated primary hypothyroidism. The pathophysiology of this phenomenon is intriguing and involves several hormonal interactions. Hypotheses of structural similarity between thyroid-stimulating hormone (TSH) and human chorionic gonadotropin (hCG) or between TSH and follicle-stimulating hormone (FSH) and luteinizing hormone (LH) have been proposed. However, the exact mechanism underlying ovarian cyst formation in patients with primary hypothyroidism remains unclear.[1,2]

Cases of multicystic ovarian appearance associated with primary hypothyroidism other than pregnancy are limited in the literature.[3,4] The most important complication potentially limiting fertility in enlarged ovaries is ovarian torsion. Herein, we present a case of ovarian enlargement complicated by chronic ovarian torsion and pituitary pseudo-macroadenoma associated with severe primary hypothyroidism.

CASE PRESENTATION

A 27-year-old gravida 2, parity 2 woman was admitted to the gynecology emergency clinic with lower abdominal pain and abnormal uterine bleeding. The patient's medical history revealed that she had autoimmune hypothyroidism since 2017. At the time of the patient's first diagnosis of hypothyroidism (2017), her TSH was 111.22 mIU/L, free triiodothyronine (FT3): 2.46 ng/L, and free thyroxine (FT4): 0.77 ng/dL. In May 2018, her anti-thyroid peroxidase (anti-TPO) antibody level was >1300 IU/mL (normal range; 0-57 IU/mL).

To cite this article: Atak Z, Oral B, Güneş E, Rahimli Ocakoğlu S, Bayram F. A Case of Primary Hypothyroidism Complicated with Pituitary Pseudo-Macroadenoma and Chronic Adnexal Torsion. Cyprus J Med Sci. 2024;9(6):450-453

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Received: 12.06.2024
Accepted: 03.09.2024

The patient was prescribed levothyroxine, but she did not take her medication regularly. Hospital records showed that the patient gave birth in 2018, but she did not attend any of her follow-up visits after the postpartum period. She presented to a local hospital in February 2022 due to fatigue; treatment for anemia with a hemoglobin level of 9.3 g/dL and antidepressant medication were prescribed for her depressive mood disorders. The results of thyroid function tests at a local hospital in March 2022 were; TSH >100.00 mIU/L (0.35-5.5), FT3: 1.51 pg/mL (2.3-4.2), FT4: 0.40 pg/mL (0.8-1.76), anti-TPO: 937.63 IU/mL (0-60), antithyroglobulin antibodies: 1.65 IU/mL (0-4.5). It was found that the patient did not start receiving the recommended treatment with levothyroxine. The first application of the patient to our hospital was on April 2, 2022. The body mass index of our patient was 25.2 kg/m^2. Physical examination revealed widespread abdominal tenderness and a mass extending above the umbilicus. Ultrasound scan showed that the endometrial thickness was 6.6 mm, the right ovary was 124x102x55 mm, and the left ovary was 135x139x80 mm in size, with mild ascites. A multicystic appearance was observed in both ovaries, mimicking ovarian hyperstimulation (Figure 1). The patient did not have a recent history of any medication. There were no signs of bradycardia or myxedema on physical examination. Until the last 2 months, the patient's menstrual history was unremarkable. She emphasized that she had heavy menstrual bleeding for the past 10 days. The laboratory findings at admission and during follow-up are summarized in Table 1. Liver and renal function tests were within the normal range during the follow-up period. Magnetic resonance imaging (MRI) of the pituitary gland revealed an 18 mm macroadenoma. Although compression of the optic chiasm was noted due to macroadenoma, no visual field defects.

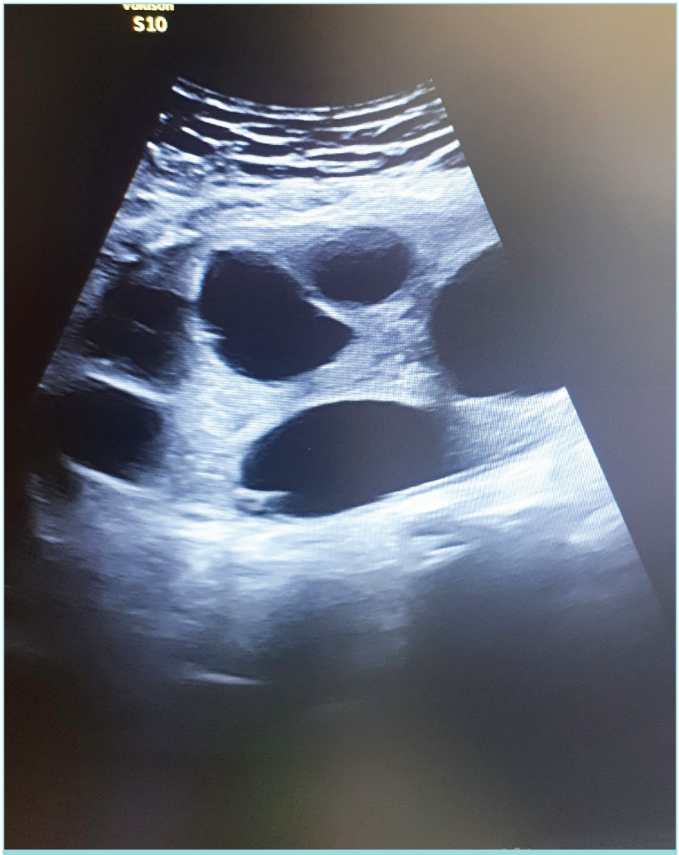

Figure 1. Ultrasonographic appearance of theca lutein cysts.

At follow-up, the hemoglobin value of the patient who experienced heavy menstrual bleeding decreased to 7.2 g/dL. For the treatment of heavy menstrual bleeding, both norethisterone acetate and tranexamic acid tablets were administered three times daily. Intravenous iron carboxymaltose was administered to the patient to treat chronic iron deficiency anemia after transfusion with erythrocyte suspension.

Levothyroxine 1x125 mg was started to treat primary hypothyroidism. At the end of 7th month of thyroxine replacement therapy, pituitary MRI revealed regression of the pseudo-macroadenoma (Figure 2).

The patient responded to treatment, and her menstrual cycle and bleeding returned to the normal range with the normalization of the thyroid function tests. Radiological assessment at the end of the 7-month follow-up period showed that the right ovary had returned to normal size. However, it was noted that the decrease in the size of the left ovary was not as significant as that of the right ovary. Additionally, due to occasional complaints of left groin pain and diminished left ovarian vascularity, the patient was scheduled for surgery with a preliminary diagnosis of ovarian torsion. However, the patient refused the surgery because of the intermittent self-resolving pain. The patient did not undergo surgery after clinical suspicion of ovarian torsion and underwent laparoscopic left oophorectomy at another medical center approximately 18 months after the primary hospital admission. The perioperative surgical note noted an adnexal mass of approximately 8,5 cm in size, in which normal ovarian tissue could not be clearly distinguished. The mass was in torsion for two complete rotations. Foci of necrosis, microcalcification, and hemorrhage were observed on histopathological examination of the oophorectomy material.

DISCUSSION

Theca lutein cysts are physiological bilateral ovarian cysts that can cause a serious increase in ovaries' size. The pathophysiology of this condition has not been clarified. In the presence of increased ovarian sensitivity, theca lutein cysts may develop as a result of prolonged or high-concentration hCG exposure. Another hypothesis is that high levels of TSH, due to their similar glycoprotein structure, may cause cyst formation in the ovaries with an FSH- and LH-like effect.[4] Although it usually accompanyes molar or multiple pregnancies, it can rarely be observed in uncomplicated singleton pregnancies.[5] Multiple ovarian cyst cases associated with primary hypothyroidism have been reported in the literature, even in the prepubertal and pubertal period.[2,6-9]

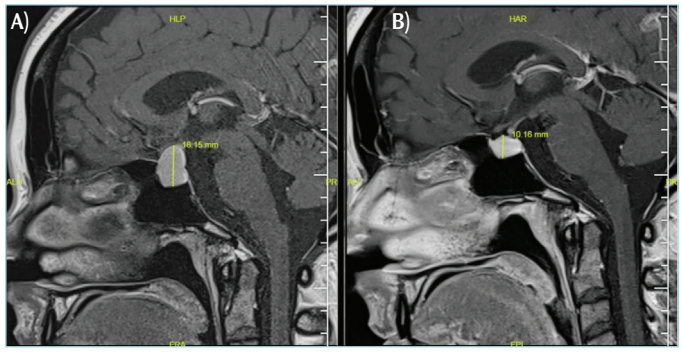

Figure 2. Contrast-enhanced magnetic resonance imaging; (A) T1A sagittal section at admission. (B) T1A sagittal section 7 months after initiating levothyroxine treatment.

Table 1. Laboratory features of the patient

	Admission	1st month	8th month	15th month	Reference range
TSH (mIU/L)	729	3.65	2.48	0.95	0.27-4.20
Free-T3 (ng/L)	1.44	5.22	3.28	3.28	2.04-4.44
Free-T4 (ng/dL)	0.59	2.59	1.6	1.81	0.93-1.71
Anti thyroglobuline antibody (IU/mL)	Normal range		Normal range		0-4.5
Anti-thyroid peroxidise antibody (IU/mL)	937.63		301		Cut-off: 60 IU/mL
FSH (IU/L)	7.8		5.2		3.5-12.5
LH (IU/L)	0.5		14		2.4-12.6
Estradiol (ng/L)	6.8		65.3		30.9-80.4
Prolaktin (µg/L)	165	91.60	45.1		4.79-23.3
GH (µg/L)	1.43		0.06		0.126-9.88
ACTH (ng/L)	34.5		48.3		7.2-63.3
Cortisol (µg/dL)	19.4	15.9	13.5		6.02-18.4
IGF-1 (ng/mL)	69.90		136		118-303
Total testosterone (µg/L)	<0.025				0.084-0.481
DHEA-SO_4 (µg/dL)	72	63			98.8-340
Total cholesterol (mg/dL)	293	190	196	239	3-200
LDL (mg/dL)	220	144	135	168	0-130
HDL (mg/dL)	40	27	46	40	45-65
Triglyceride(mg/dL)	166	95	74	155	0-200
Hemoglobin (g/dL)	8.6	10.2	9.6	9.7	11.9-14.6
CA-125 (IU/mL)	15.6	15.2	10.9	7.7	0-35
CA-19-9 (IU/mL)	4.9	5.3	6.7	3.66	0-39
CEA (IU/mL)	2.2	0.9	1.4	1.11	-
LDH (IU/L)	212	188		173	135-214
AFP (µg/L)	3.44	1.79	1.63	1.82	0-8.3

TSH: Thyroid-stimulating hormone, Free-T3: Free-triiodothyronine, Free-T4: Free-thyroxine, FSH: Follicle-stimulating hormone, LH: Luteinizing hormone, GH: Growth hormone, ACTH: Adrenocorticotropic hormone, IGF-1: Insulin-like growth factor 1, DHEA-SO4: Dehydroepiandrosterone sulphate, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, CA-125: Cancer antigen-125, CA-19-9: Carbohydrate antigen-19-9, CEA: Carcinoembryonic antigen, LDH: Lactate dehydrogenase, AFP: Alpha-fetoprotein.

Ovarian masses associated with primary hypothyroidism are rarely observed in non-pregnant adult women.[10]

Thyroid function tests should be considered, especially in the presence of bilateral multiple ovarian cysts that mimic ovarian hyperstimulation syndrome. Cases in which the TSH value increased to 4191.5 mIU/L (normal, 0.47-5.01) have also been reported in the literature.[1] Our patient's TSH level upon admission was 729 mIU/L, which decreased to its normal level in the 1st month of thyroxine replacement therapy. As in our case, pituitary pseudo-macroadenoma can also be observed in these patients.[11]

Despite advances in imaging, it is still challenging to distinguish pituitary hyperplasia from pituitary adenomas. In patients with primary hypothyroidism, reactive pituitary hyperplasia can cause hyperprolactinemia, but prolactin secretion usually normalizes after the initiation of levothyroxine therapy. In the present case, prolactin levels returned to normal with levothyroxine replacement without any dopamine agonist therapy, and the appearance of macroadenoma in the pituitary gland regressed. In our case, while the laboratory parameters improved rapidly, it took seven months for the pituitary pseudo-macroadenoma to regress. Our clinical case highlights the importance of hormonal evaluation in the context of pituitary mass to reach a correct diagnosis and prevent unnecessary intervention.

There are also cases of chronic adnexal torsion reported previously.[12] If the time from diagnosis of ovarian torsion to surgery is longer than three days, it is defined as chronic adnexal torsion. Cases lasting up to 210 days between the onset of pain and diagnosis have been reported in the literature.[13] Elevated white blood cell counts and C-reactive protein levels, which are usually observed in ovarian torsion, were not observed during our patient's follow-up. In our case, the intraoperative appearance of the left adnexa and histopathological findings also supported chronic torsion.

In conclusion, knowledge that ovarian and pituitary enlargement may result from severe hypothyroidism can help avoid unnecessary medical or surgical procedures. While improvement in laboratory parameters is observed in a short period, improvement via imaging may take longer. If there is no regression in ovarian size during follow-up, ovarian torsion should be suspected.

MAIN POINTS

- In this study, we present a case of ovarian enlargement complicated with chronic ovarian torsion and pituitary pseudo-macroadenoma associated with severe primary hypothyroidism.

- Multidisciplinary approach protects the patient from unnecessary surgery and medical treatment.
- In cases of primary hypothyroidism, levothroxine treatment alone is sufficient for the regression of pituitary macroadenoma and ovarian theca luterine cysts.

ETHICS

Informed Consent: Written informed consent was obtained from the patient.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Z.A., E.G., F.B., Concept: Z.A., Design: Z.A., B.O., Data Collection and/or Processing: Z.A., S.R.O., B.O., Analysis and/or Interpretation: S.R.O., B.O., Literature Search: Z.A., E.G., S.R.O., F.B., Writing: Z.A., E.G., F.B.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The author declared that this study has received no financial support.

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