CAS CLINIQUE / CASE REPORT

MULTICYSTIC OVARIES IN UNTREATED PEDIATRIC HYPOTHYROIDISM
A Risk Factor for Ovarian Torsion

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Naffaa L, Birjawi G, Baassiri A, Jarjoura P. Multicystic ovaries in untreated pediatric hypothyroidism: a risk factor for ovarian torsion. J Med Liban 2018 ; 66 (3) : 165-169.

ABSTRACT • Background : In this case report, we hope to increase awareness of pediatric hypothyroidism as a cause of multicystic ovaries which increases the risk for ovarian torsion. By treating hypothyroidism, we can prevent such an occurrence. **Case** : A 13-year-old hypothyroid female presented with right lower quadrant abdominal pain and bilateral multicystic ovarian enlargement on sonography. There was a suspicion of right ovarian torsion which was confirmed by laparoscopy. Her TSH level was 997 µU/mL. The right ovary was significantly reduced in size after drainage, and ovariopexy was successfully done as the ovary was still viable after detorsion. The left ovariopexy failed as left ovary remained too large after drainage. Patient's levothyroxine dose was increased from a daily dose of 25 µg to 44 µg. Repeat ultrasound six weeks later showed a decrease in ovarian size and volume. **Conclusion** : Awareness of such an entity would spare a pediatric patient the complications of undertreated hypothyroidism such as multicystic ovaries which can be complicated by ovarian torsion. Those ovarian cysts tend to resolve with thyroid hormone replacement therapy and therefore prevent an unnecessary surgery and a serious complication like an ovarian torsion. Also, any pediatric patient diagnosed with polycystic ovaries should be screened for hypothyroidism.

Keywords : polycystic ovaries; hypothyroidism; pediatrics

Naffaa L, Birjawi G, Baassiri A, Jarjoura P. Ovaires polykystiques dans l'hypothyroïdie pédiatrique: un facteur de risque de torsion ovarienne. J Med Liban 2018 ; 66 (3) : 165-169.

RÉSUMÉ • Contexte : Avec ce cas clinique, nous espérons éclairer le public sur l'hypothyroïdie pédiatrique en tant qu'étiologie des ovaires polykystiques qui augmente à son tour le risque de torsion ovarienne. En traitant l'hypothyroïdie, les torsions ovariennes peuvent être prévenues. **Cas clinique** : Une patiente de 13 ans avec hypothyroïdie se présentant pour douleur à la fosse iliaque droite. L'échographie pelvienne montre une hypertrophie ovarienne polykystique bilatérale avec suspicion de torsion ovarienne droite confirmée en cœlioscopie. Le niveau sérique de TSH était 997 µU/mL. Après ponction et drainage, la taille de l'ovaire droit s'est réduite significativement. L'ovariopexie droite s'est faite avec succès puisque l'ovaire était toujours viable après détorsion. L'ovariopexie gauche n'avait pas réussi, l'ovaire étant resté partiellement hypertrophié après ponction. La dose de lévothyroxine a été augmentée de 25 µg/j à 44 µg/j. L'échographie répétée 6 semaines plus tard a montré une diminution de l'ovaire en taille et volume. **Conclusion**: Il est impératif d'être conscient de cette entité pour éviter les conséquences d'une hypothyroïdie mal traitée comme les ovaires polykystiques compliqués par torsion ovarienne. Les kystes ovariens ont tendance à se résoudre avec le remplacement hormonal thyroïdien, ce qui évite par conséquent les chirurgies non nécessaires et une complication grave telle que la torsion ovarienne. Ainsi, chaque patiente pédiatrique chez qui on a fait le diagnostic d'ovaires polykystiques doit être évaluée pour hypothyroïdie.

Mots-clés : ovaires polykystiques; hypothyroïdie; pédiatrie

INTRODUCTION

Thyroid hormones play a pivotal role in the growth and development of children. There are several etiologies for pediatric hypothyroidism. All of them share the same deleterious outcome including height reduction due to slow skeletal growth, constant fatigue, impaired memory, concentration difficulties, depression, abnormal menses, precocious puberty, vaginal bleeding, and recurrent ascites [1,2].

Bilaterally enlarged multicystic ovaries secondary to hypothyroidism have been rarely reported in adults [3-6] and pediatric age group. The review of the literature resulted in fewer than 10 cases reported to date [7,8]. In addition, acute ovarian torsion, as a complication of enlarged multicystic ovaries secondary to hypothyroidism, is rarely encountered in the pediatric age group [9,10].

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We describe a 13-year-old girl with insufficiently treated hypothyroidism complicated by enlarged cystic ovaries, presenting with acute right abdominal pain secondary to torsion of the right ovary. We hope to increase awareness of such an occurrence in the pediatric age group with this rare case report and review of the literature.

CASE REPORT

A 13-year-old girl was referred from family medicine to the endocrinology clinic for persistent fatigue, weight gain and poor height growth over the last two years (Table I).

History and physical examination were done. In addition, lab results that were requested from the family medicine specialist were reviewed. She was diagnosed with hypothyroidism and was started on levothyroxine 25 µg daily. It was expected that the patient would require a higher dose, however, not promptly initiated to prevent its side effects including headache and blurry vision. Thyroid

function tests were to be obtained every two weeks in addition to monitoring glucose level (Table I).

Three weeks later, the patient presented to the emergency department (ED) with a progressive severe right-sided abdominal pain, which started on the same day, associated with more than ten episodes of vomiting. Lab tests were requested and radiological studies were done. The findings were highly suspicious for right ovarian torsion and patient was taken to the operating room. Laparoscopy confirmed our suspicion and the appropriate operation was done. The hospital recovery course was uneventful. Patient's levothyroxine dose was increased from a daily dose of 25 μg to 44 μg (Table II). On her six weeks follow-up after surgery, patient was feeling much better and a repeat pelvic ultrasound showed a decrease in ovarian size (Table III).

TABLE I. TIMELINE OF EVENTS AT THE FAMILY MEDICINE SPECIALIST AND ENDOCRINOLOGY CLINIC

Event	At Family Medicine Specialist	At Endocrinology Clinic
Chief Complaint	Persistent fatigue Weight gain Poor height growth over the last two years	Persistent fatigue Weight gain Poor height growth over the last two years
History	N/A	Unilateral galactorrhea of the left breast + whitish discharge Facial flushing Dry skin Joint pain Intermittent constipation No difficulty in sleeping No change in appetite No change in school performance No change in vision or voice No dysphagia No heat or cold intolerance Psychological evaluation was negative Menarche & adrenarche were at 11 years of age
Physical Examination	N/A	Height: 141 cm (3rd percentile) Weight: 53.3 kg (93rd percentile) Body Mass Index BMI: 26.81 kg/m^2 Vitals Blood Pressure: 110/70 mmHg Pulse: 84 bpm No pallor or lethargy Acanthosis nigricans was present involving the posterior neck, but no striae or hyperpigmentation Thyroid examination No palpable or enlarged nodules Rubbery in consistency Adult axillary hair was noted Breasts & pubic hair were Tanner Stage 4 Galactorrhea of the left breast
Lab Results	Hemoglobin Alc 6.3% Thyroid stimulating hormone (TSH) 997 μU/m Thyroxine (T4) 0.19 ng/dL Glucose: 92 mg/dL Aspartate aminotransferase (AST): 38 U/L Alanine aminotransferase (ALT): 56 U/L	Follicular stimulating hormone (FSH): 18 mU/mL Luteinizing hormone (LH): 16 IU/mL Prolactin (PRL): 12.5 mg/mL Estradiol (E2): 1.6 pg/mL Testosterone: 2.3 pg/mL Thyroid peroxidase antibodies: 23 IU/mL
Radiological Studies	–	Thyroid Ultrasound: Hypoechogenic heterogeneous echostructure with micronodules Thyroid volume: 47 mL
Diagnosis	–	Hypothyroidism in favor of Hashimoto thyroiditis
Treatment	Referred to Endocrinology Clinic	Levothyroxine 25 μg daily

TABLE II. TIMELINE OF EVENTS AT THE EMERGENCY DEPARTMENT

Event	Three weeks later at the Emergency Department
Chief Complaint	Progressive severe right-sided abdominal pain which started on the same day Associated with 10 episodes of vomiting
History	No fever • Chills • No nausea or vomiting • Decreased appetite • Decreased urine output
Physical Examination	Abdomina examination: Right lower quadrant & Suprapubic tenderness
Lab Results	Complete blood count (CBC) • Leukocytes count: 14.4 x 10^3/mm^3 Blood chemistry • BUN: 11 mg/dL • Creatinine 0.54 mg/dL • Sodium: 138 mEq/L • Potassium: 3.6 mEq/L • Chloride: 112 mEq/L • Calcium: 8.1mg/dL • Carbon dioxide: 18.9 mEq/L • Anion gap: 7.1 mEq/L• Glucose: 105 mg dL Urine analysis: negative Urine pregnancy test: negative
Radiological Studies	Ultrasound examination of the pelvis (Cf. Figure 1) Right ovary: • Location: on the right of the bladder • Size: 7.5 x 6 x 8.6 cm • Volume: 202 mL • Cysts: 8-10 Left ovary: • Location: midline behind bladder base • Size: 6.2 x 4.3 x 6.9 cm • Volume: 96 mL • Cysts: 5 Spectral waveform of right ovary (Cf. Figure 2): Increased diastolic flow with RI of 0.55 compared to the left ovary
Diagnosis	Right ovarian torsion
Treatment	Surgical: laparoscopy • Right ovary: Cysts drainage + Ovariopexy • Left ovary: Cysts drainage only Medical: levothyroxine 44 μg daily

TABLE III
ULTRASOUND FINDINGS ON FOLLOW-UP

Findings	Right ovary size	Left ovary size
Preoperative	7.5 x 6 x 8.6 cm	6.2 x 4.3 x 6.9 cm
Follow-up	3.3 x 2 x 4.1 cm	2.2 x 1.7 x 3.1 cm
Decrease in ovarian sizes	4.2 x 4 x 4.5 cm	4 x 2.6 x 3.8 cm

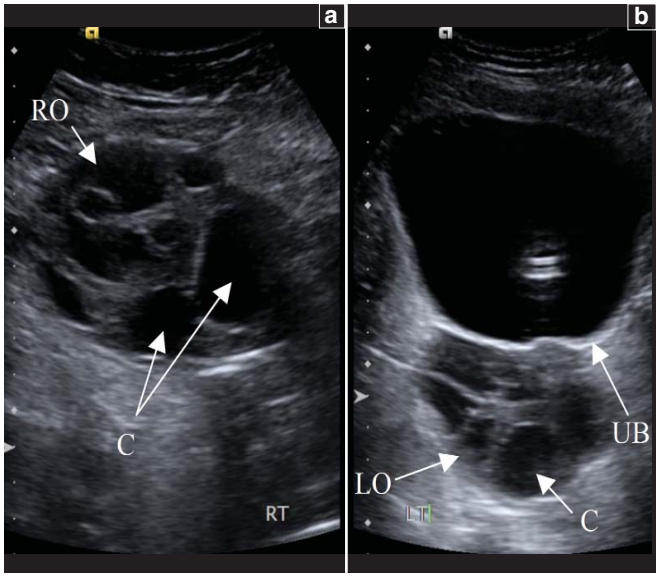

Figure 1
Transverse gray scale ultrasound image of the pelvis.
Image [**a**] shows an enlarged right ovary (RO) containing multiple cysts (C), largest measuring 2 cm in greatest dimension.
Image [**b**] shows an enlarged left ovary (LO) containing multiple cysts (C) located behind the urinary bladder (UB) in the midline.

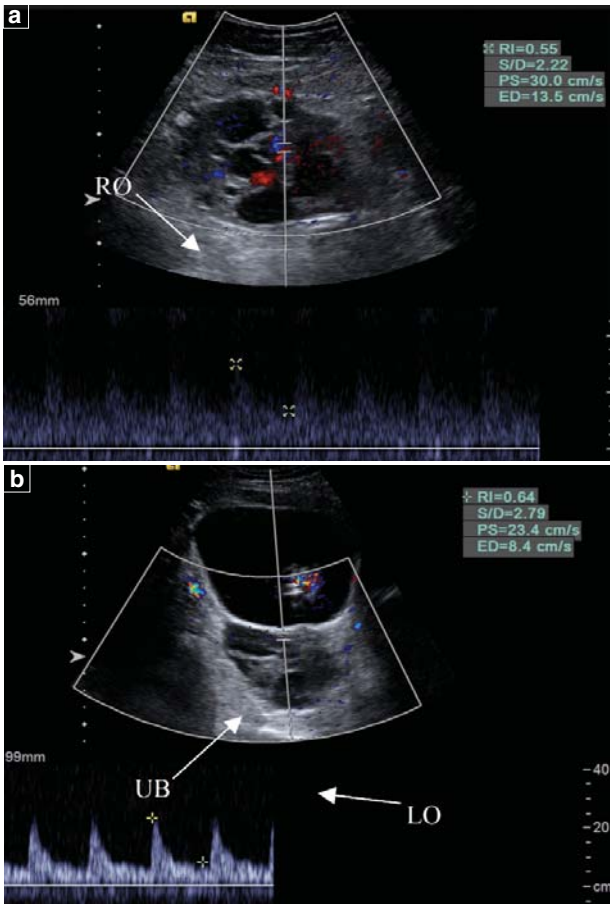

Figure 2. Color doppler ultrasound examination of the right ovarian (RO) parenchyma in [**a**] shows a relatively increased diastolic flow with an RI of 0.55 indicating an element of ischemia compared to normal arterial spectral waveform and RI in the left ovary (LO) in [**b**].

DISCUSSION

A 13-year-old hypothyroid patient presented with right lower quadrant abdominal pain and bilateral multicystic ovarian enlargement on sonography. The significantly enlarged right ovary and abnormal spectral arterial waveforms were highly suspicious for torsion which was confirmed by laparoscopy. Aligning with our patient's case, a recent systematic review of ovarian torsion in the pediatric population identified right lower abdomen as the most common location of pain [11]. It has been suggested that right-sided torsion predominance may be due to the ample space surrounding the right ovary in comparison to the left ovary which is confined by the occupation of the sigmoid colon [12]. Another theory is that since the right utero-ovarian ligament is physiologically longer than the left, ovarian torsion is more probable to occur on the right.

The presence of bilateral ovarian blood flow may have been deceptively reassuring. This may be explainable on the basis of intermittent ovarian torsion. However, Pena *et al*. documented that while Doppler sonography had a specificity of 100%, its sensitivity was 60% [13]. According to Albayram *et al*., absence of arterial blood flow was detected in only 73% of cases. Moreover, normal arterial and venous flow was demonstrated in one case (6%) out of a total of 15 [14]. There is no consensus yet on the true sensitivity and specificity of color Doppler sonography in predicting ovarian torsion. The dual ovarian arterial blood supply, the ovarian artery and branches from the uterine artery, may account for preservation of arterial blood flow [15]. Therefore, normal blood flow by Doppler sonography does not rule out ovarian torsion.

In order to establish a suspicion index for ovarian torsion in the pediatric population, one needs to be familiar with the predisposing factors. These primarily include ovarian tumors and syndromes that result in multiple or large heavy cysts such as polycystic ovarian syndrome (PCOS) and pediatric hypothyroidism. Nevertheless, it is crucial to keep in mind that appendicitis and ruptured ovarian cyst may mimic ovarian torsion. The presentation of precocious puberty and adnexal mass is highly suspicious of an estrogen-secreting ovarian tumor such as a juvenile granulosa cell tumor [16]. Rarely may CA-125 be elevated [17]. In regards to PCOS, there is no general consensus among medical societies on the definitive diagnostic criteria of PCOS. Nevertheless, polycystic ovaries alone are a nonspecific finding and can be seen in women with no endocrine or metabolic abnormalities. The 2003 Rotterdam Consensus Criteria required two out of the following three conditions: 1) oligo- or amenorrhea, 2) clinical or biochemical signs of hyperandrogenism, 3) polycystic ovaries [18]. Our patient did not have signs of precocious puberty or signs of hyperandrogenism. As such, we were left with hypothyroidism as the cause of ovarian enlargement and formation of the ovarian cysts.

Hypothyroidism may result in galactorrhea as in our patient's case. This is a consequence from the high levels of thyrotropin-releasing hormone (TRH) which induce the release of prolactin alongside thyroid stimulating hormone (TSH). Furthermore, through animal studies, it has been demonstrated that hypothyroidism induces collagen deposition within the ovarian intracellular matrix [19]. Hansen *et al*., were first to document myxedematous-type infiltrates in the ovary of a 16-year-old girl with primary hypothyroidism [3]. It is necessary to recognize that ovarian enlargement alone is a risk factor for ovarian torsion. Moore *et al*., reported ovarian enlargement as the most consistent sonographic finding in ovarian torsion [20].

Several theories have been proposed concerning the mechanism by which hypothyroidism may induce the formation of ovarian cysts. At first it was hypothesized by Van Wyk and Grumbach that primary hypothyroidism would result in decreased feedback to the pituitary. This will result in a hyperplastic pituitary that may be releasing high levels of TRH as well as gonadotropins, mainly follicle-stimulating hormone (FSH) and luteinizing hormone (LH) [21]. However, there have been cases that reported normal levels of gonadotropins [22]. A second theory is that TSH may sensitize the ovaries to gonadotropin stimulation [23]. A third possible mechanism is that certain FSH receptor (FSHR) mutations may render them to be able to nonspecifically respond to other tropic hormones such as TSH [24]. A fourth mechanism postulated is that significant levels of TSH can bind to human FSHR and lead to activation of follicular cells. Anasti *et al*. showed that in an in vitro human FSHR bioassay, recombinant human TSH (rec-hTSH) can elicit a dose-dependent cyclic adenosine monophosphate (cAMP) response. However, the concentration of rec-hTSH needed for half-maximal stimulation was several logs greater than that of human FSH [25]. This theory was supported by similar findings in a study carried out by De Leener *et al*. Unlike the third postulation, De Leener *et al*. observed rec-hTSH activation of wild-type human FSHR with no mutations whatsoever [26].

CONCLUSION

In summary, the work-up of a pediatric patient presenting with enlarged multicystic ovaries should include a measurement of thyroid hormone levels. Rarely does pediatric hypothyroidism present with ovarian torsion or ovarian cyst rupture. Increased awareness of such an entity would spare a child an unnecessary surgery for ovarian cysts since they tend to resolve with thyroid hormone replacement therapy and therefore prevent from ovarian torsion.

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