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Case Report

Interdisciplinary Care and a Focus on Fertility Preservation When Multi-cystic Ovaries Cause Ovarian Torsion: A Case of a 9-year-old Girl with Severe, Undiagnosed Hypothyroidism

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A B S T R A C T

Background: Ovarian torsion can occur in Van Wyk Grumbach syndrome, a disorder characterized by severe primary hypothyroidism and ovarian enlargement. To date, all documented cases of torsion in this setting describe oophorectomy, which has significant hormonal and fertility implications.

Case: A 9-year-old pubertal girl presented to the emergency room with abdominal pain. Magnetic resonance imaging demonstrated bilateral, multi-cystic ovaries. Operative laparoscopy confirmed unilateral adnexal torsion, and detorsion without oophorectomy was accomplished. Postoperative laboratory tests revealed severe primary hypothyroidism. Ovarian size was reduced with hormone replacement therapy.

Summary and Conclusion: This case demonstrates that prompt interdisciplinary intervention and awareness of severe hypothyroidism as a cause of ovarian torsion related to enlarged, multi-cystic ovaries may reduce the rate of oophorectomy, allowing preservation of pediatric patients' future fertility, and reducing morbidity postoperatively through prompt, long-term thyroid supplementation.

Introduction

Ovarian torsion of an enlarged ovary around a vascular pedicle is a relatively common gynecologic emergency among adolescents and adults[1] that can have important clinical implications for future hormone production and fertility due to related ischemia and the potential loss of ovarian function. In menstruating girls, the ovaries can be enlarged due to functional and non-functional masses, that can be benign or, less commonly, malignant. Non-malignant bilateral large multi-cystic ovaries is a relatively uncommon occurrence in adolescents, as this is usually only seen after significant gonadotropin stimulation. When a large multi-cystic ovary is noted in a young girl, hyperstimulation due to severe primary hypothyroidism, as described in Van Wyk Grumbach syndrome, should be part of the differential diagnosis. In this syndrome, elevated thyroid stimulating hormone (TSH) acts on the follicle stimulating hormone (FSH) receptor resulting in downstream elevation in estrogen and precocious pubertal changes. This is a treatable and reversible condition, usually with resolution of precocious puberty and ovarian enlargement after treatment with levothyroxine.

This case describes undiagnosed Van Wyk Grumbach syndrome manifesting as acute abdominal pain, large bilateral multi-cystic ovaries and unilateral ovarian torsion, demonstrating the need for focus on fertility preservation.

Case

A pubertal girl who was 9 years 11 months of age and of white ethnicity, with a history of morbid obesity (body mass index [BMI] > 99%) and short stature (<1%), presented to the emergency department with a 4-day history of worsening right lower-quadrant abdominal pain and fever. Her mother reported that she had had irregular bleeding since age 7 years. Physical examination showed a girl 4 feet tall in moderate distress with acanthosis nigricans of the neck and bilateral axillary folds, Tanner stage 4 breasts, Tanner stage 2 pubic hair, and diffuse tenderness with peritoneal signs on abdominal examination. Initial laboratory tests were notable for leukocytosis (white blood cell count 16.2 × 10^9/L), mild anemia (hemoglobin 11.2 g/dL), and elevated C-reactive protein (CRP; 19.2 mg/L). She underwent magnetic resonance imaging (MRI) for presumed appendicitis (Figure 1); however, this demonstrated a normal appendix and instead showed enlarged multi-cystic lesions of both ovaries (right: 6.6 × 7.4 × 5.2 cm; left: 9.4 × 12.2 × 4.6 cm) with swirling of the vascular pedicle on the right (Figure 2, white arrow), suspicious for

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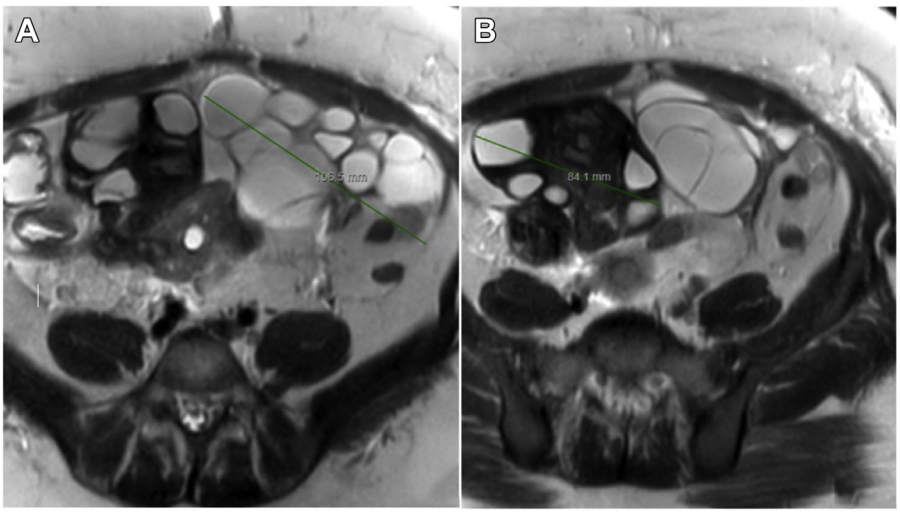

Fig. 1. Pre-operative non-contrast MRI abdomen/pelvis showing bilateral enlarged, multicystic ovaries. (A) Left overy, markedly enlarged multicystic structure appearing to arise from the left ovary, with a dominant solid component; (B) Right ovary, enlarged cystic structures with markedly T2 hypointense parenchyma, suggestive of internal hemorrhage. Written consent to photography/imaging for the purpose of publication was obtained.

torsion. The decision was made to proceed with emergent diagnostic laparoscopy for suspected ovarian torsion by the pediatric surgery team. Tumor markers were drawn and pending at the time of her surgery. Intraoperative findings confirmed preoperative imaging with an ischemic tube and a multi-cystic torsed right ovary (measuring approximately 14 × 7.5 cm). The left ovary also appeared multi-cystic (measuring approximately 14 × 5 cm) but was well perfused, without torsion. Gynecology was consulted intraoperatively, and advised detorsion without oophorectomy. Because of the size of the ovaries and concern about the ability to safely proceed with laparoscopy, a laparotomy was performed with detorsion of the 4-times-torsed right ovary. Cystectomy and oophoropexy were not attempted because of the large edematous multicystic ovaries (Figure 3). Pelvic washings demonstrated numerous acute inflammatory cells but no malignant cells. Tumor marker results, available postoperatively, were notable for an elevated CA-125 (87 U/mL), inhibin A (379 pg/mL), and inhibin B (1975 pg/mL).

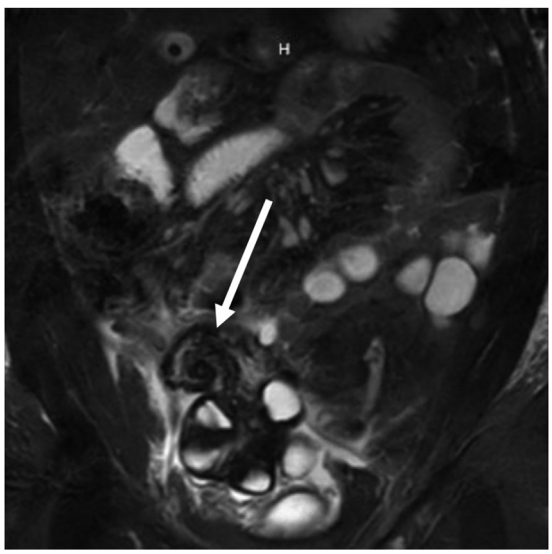

Fig. 2. Pre-operative, non-contrast MRI abdomen/pelvis with “swirling” of the vascular pedicle of the right ovary (white arrow). Written consent to photography/imaging for the purpose of publication was obtained.

Immediately postoperatively, hormonal testing was initiated, given the patient's isosexual precocious pubertal development, 2-year history of irregular bleeding and short stature. Workup revealed profound hypothyroidism (thyroid-stimulating hormone [TSH] 520.8 mIU/L) with elevated thyroid peroxidase antibodies of 2,704 IU/mL and an elevated prolactin of 117 ng/mL. A skeletal survey showed a significantly delayed bone age, and a brain MRI demonstrated an avidly enhancing sellar/suprasellar mass (1.4 × 1.6 × 1.9 cm) consistent with a pituitary macroadenoma secondary to hypertrophy of thyrotrophs. Given significant acanthosis nigricans on examination, a 2-hour glucose tolerance test was performed, demonstrating impaired glucose tolerance. Through interdisciplinary care coordination with pediatric endocrinology, the patient was diagnosed with Van Wyk Grumbach syndrome, after a leuprolide stimulation test performed postoperatively confirmed the absence of gonadotropin-dependent precocious puberty. She was discharged home on levothyroxine with a plan for immediate and long-term endocrinology follow-up. Her parents noted a subsequent improvement in mood, cognition, and school performance with levothyroxine supplementation. Serial pelvic ultrasound showed that bilateral ovaries were progressively decreased in size at both 3 weeks (left: 8.5 × 4.0 × 11.2 cm; right: 11.0 × 5.5 × 8.9 cm) and 4 months (left: 5.8 × 4.9 × 2.3 cm; right: 4.4 × 3.9 × 3.0 cm) postoperatively. At 4 months postoperatively, peripheral follicles were seen in the left ovary; however, follicles within, and vascular flow to, the right ovary were not noted. At 1-year follow-up, the parents reported that the patient's previously irregular bleeding had stopped entirely with initiation of levothyroxine treatment.

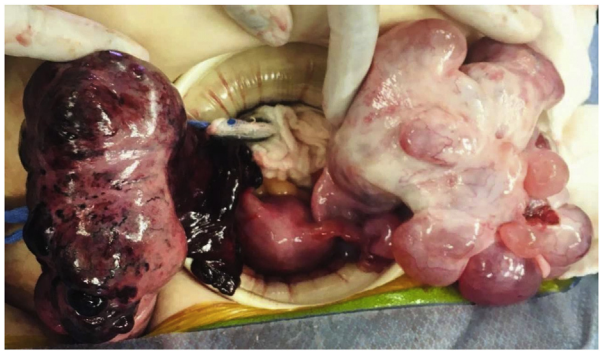

Fig. 3. Intraoperative photograph demonstrating multicystic and enlarged ovaries immediately after detorsion of right ovary. Written consent to photography/imaging for the purpose of publication was obtained.

Summary and Conclusion

This case demonstrates that an interdisciplinary approach in the setting of torsion due to an uncommon phenomenon, such as enlarged multi-cystic ovaries caused by hypothyroidism, can lead to a thoughtful patient workup and outcome.

The association of juvenile hypothyroidism with isosexual precocious puberty, delayed bone age, and multicystic ovarian involvement was first described by Judson J. Van Wyk and Melvin M. Grumbach in 1960.[2] Although there have been several documented case reports of hypothyroidism leading to ovarian enlargement, there are only 2 pediatric (ages 5 and 12 years) cases and 1 adult case in the literature that report ovarian torsion at the time of presentation.[3–5] All of these cases led to unilateral oophorectomy of the affected ovary, although this is a reversible condition.

In this case, the decision was made to leave the ovary in place, as it is crucial that oophorectomy, in the setting of torsion in a young girl, be avoided unless strictly necessary (ie, in the setting of malignancy or necrosis in which the ovarian tissue is falling apart).[1] There is significant evidence to support ovarian detorsion over oophorectomy for the management of pediatric ovarian torsion—which can often be safely accomplished laparoscopically although in our case was performed via laparotomy because of adnexal size—with a high likelihood that salvaged ovaries will remain viable, regardless of gross appearance, at the time of surgery.[1] It is unclear how long an ovary can survive after it has been torsed, particularly given this organ's collateral blood supply. There has been a suggestion of decline in function after 72 hours; however, there is no clear cut-off. Although oophorectomy was previously suggested to reduce the proposed morbidity of a necrotic ovary left in place, there is no evidence that ovarian conservation is associated with an increased rate of subsequent complication.[6] In this case, although it is unknown whether the torsed right ovary will be functional in the future, the decision to refrain from oophorectomy at the time of surgery led neither to postoperative morbidity nor the need for reoperation.

Although benign functional cysts and teratomas are the most common cause of torsion, accounting for more than one-half of pediatric and adolescent adnexal torsion cases, in as many as 46% of cases there is no inciting mass or cyst, and malignancy in this age group is rare.[1] As in this case, bilateral, enlarged, multi-cystic ovaries in a young girl should prompt consideration and evaluation for an endocrinopathy and, much less commonly, malignancy. Thus, testing for hypothyroidism (TSH and free thyroxine or T4) should be included in the initial evaluation. Additionally, although tumor markers may be useful in assessing for malignancy, elevations in inhibin[7] and α-fetoprotein[8] can also be seen in Van Wyk Grumbach syndrome, and CA-125 can be elevated in young women in a variety of settings (eg, endometriosis, inflammation, etc). Thus, we propose an algorithm of initial thyroid testing prior to, or in conjunction with, tumor markers preoperatively in multi-cystic ovaries in young women, to reduce the likelihood of unnecessary oophorectomy in patients with elevated tumor markers. Emergent surgery should not be delayed while waiting for results, and elevated tumor markers alone should not motivate oophorectomy in this age group when bilateral, multi-cystic ovaries are present. Instead, a decision to proceed with oophorectomy in a pediatric or adolescent patient should be made based on imaging and intraoperative findings with a disintegrating ovary or changes suggestive of malignancy (for example, ascites, peritoneal studding), ideally in conjunction with a complete workup excluding an underlying endocrinopathy, to avoid an unnecessary oophorectomy.

In this case, multi-disciplinary teamwork, with intraoperative consultation by gynecology, enabled the surgical team to proceed with detorsion without oophorectomy in this young patient. Additionally, immediate postoperative consultation, and subsequent close follow-up, with pediatric endocrinology is critical in the initial evaluation, management, and ongoing surveillance of thyroid function in these patients. Notably, unlike most structural causes of ovarian enlargement leading to adnexal torsion in this young population, exogenous levothyroxine supplementation alone allows for resolution of ovarian enlargement and long-term-recovery in these patients. Moreover, other cases have illustrated that tumor marker derangements also improve with exogenous levothyroxine supplementation.[7,8] Thus, when a pediatric patient presents with acute pain and bilateral ovarian enlargement, a diagnosis of Van Wyk Grumbach syndrome should be considered and multi-disciplinary care initiated. In these cases, following prompt diagnostic laparoscopy for identification and treatment (de-torsion) of ovarian torsion, emphasis is placed on medical management of hypothyroidism rather than surgical management with oophorectomy.

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