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A CASE OF OVARIAN HYPERSTIMULATION SYNDROME WITH HYPOTHYROIDISM IN A 14-YEAR-OLD FEMALE – VAN WYK GRUMBACH SYNDROME.

Paediatric Medicine

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ABSTRACT

Introduction: Van Wyk Grumbach Syndrome (VWGS) is a rare disorder that manifests in pre-pubertal females with long-standing untreated hypothyroidism. This condition is characterized by delayed skeletal growth, precocious pseudopuberty, and bilateral multi-cystic ovaries. VWGS, caused by elevated thyroid-stimulating hormone (TSH) levels, mimics the presentation of other gynecological disorders, often complicating diagnosis. **Case Presentation:** We report the case of a 14-year-old female who presented with gradually increasing painless abdominal distension, short stature, and bilateral multi-cystic ovarian masses. The patient had a history of early menarche at age 9, with no abnormal vaginal discharge. Physical examination revealed Tanner stage 2 thelarche, a palpable mobile mass in both iliac fossae, and a dull facial expression. Laboratory investigations revealed highly elevated TSH levels (1400 uIU/l) with low T3 and thyroxine levels, confirming the diagnosis of severe hypothyroidism. Imaging studies confirmed bilateral multi-cystic ovaries. **Management:** The patient was started on levothyroxine replacement therapy, leading to regression of the ovarian cysts. No surgical intervention was required. **Conclusion:** Van Wyk Grumbach Syndrome must be considered in young females presenting with ovarian cysts and delayed growth. Timely diagnosis and initiation of thyroid hormone replacement can prevent unnecessary surgeries and result in complete resolution of symptoms.

KEYWORDS

Hypothyroidism; Ovarian Hyperstimulation Syndrome; Van Wyk Grumbach Syndrome; Precocious Puberty; Thyroid Hormone Replacement Therapy

INTRODUCTION

Van Wyk Grumbach Syndrome (VWGS) is a rare and intriguing disorder that represents a unique intersection of endocrinology and gynecology, particularly seen in pre-pubertal girls.[1] It is characterized by the coexistence of long-standing untreated hypothyroidism, delayed skeletal growth, and the surprising appearance of precocious pseudopuberty, often accompanied by bilateral multi-cystic ovaries and unexplained vaginal bleeding.[2] This syndrome, first described in 1960, is primarily driven by elevated levels of thyroid-stimulating hormone (TSH), which mistakenly stimulate the ovaries, leading to ovarian hyperstimulation without the expected increase in sex hormone levels typically seen during puberty.[3]

The hallmark of Van Wyk Grumbach Syndrome is a clinical paradox: patients exhibit signs of sexual maturity, such as menstrual-like bleeding, despite delayed overall growth and bone development.[4] This unusual presentation makes the condition difficult to diagnose early, often leading to misinterpretation as early-onset puberty or other gynecological issues.[5] The long-standing untreated hypothyroidism not only results in delayed skeletal maturation but also the development of large ovarian cysts, which may be mistaken for more common ovarian pathologies.[6]

In this report, we describe a 14-year-old girl who was diagnosed with Van Wyk Grumbach Syndrome (ovarian hyperstimulation syndrome) as a result of untreated hypothyroidism. The patient had delayed skeletal development, multicystic ovaries, and vaginal hemorrhage, among other characteristic symptoms. This case is noteworthy because it shows how severe hypothyroidism may cause this uncommon illness and its peculiar gynecological symptoms if left untreated.

The purpose of this case is to highlight how young females who arrive with ovarian cysts and unusual pubertal development should have hypothyroidism as a possible underlying cause. By conducting this study, we seek to increase public awareness of Van Wyk Grumbach Syndrome and to promote prompt hypothyroidism diagnosis and treatment in order to avert these problems.

Case Presentation

The gynecological department received a referral for a 14-year-old girl who had been complaining of painless abdominal distension that had been steadily rising for the previous six months. The patient had a history of regular menstrual cycles, no abnormal vaginal discharge, and an early menarche at the age of 9. She was short in stature and had previously been evaluated for bilateral solid cystic adnexal masses with significant ascites, raising concerns about a potential malignant ovarian lesion.

Before a scheduled surgical operation to address her ovarian cysts, the patient was sent to us for a second opinion and to rule out ovarian cancer. After reviewing her medical history in more detail, no noteworthy anomalies were found. 2.6 kg was her birth weight when she was delivered at 37 weeks of pregnancy. Her parents noticed her lack of interest in physical activity, easy fatigability, and cold intolerance when she was 7 years old. The patient's mother noticed the commencement of menstruation over the previous three months, coupled with the growth of breast tissue and abdominal enlargement, four months before the patient presented. There was no history of consanguineous marriage, autoimmune illness, or premature puberty in the family.

Physical Examination

The patient's height of 120 cm (below the third percentile for her age) and weight of 35 kg (below the third percentile) were accompanied with a lifeless look. She measured 85/55 mm Hg for blood pressure and 58 beats per minute for heart rate. There was no pubic hair, the clitoris, labia, and anal opening were all well-developed, and there were indications of thelarche (Tanner stage 2). She could not feel her thyroid gland. During the abdominal examination, a hard, non-tender, movable mass measuring 3–4 cm was felt in both iliac fossae. This mass was also felt during the per-rectal exam. Abdominal palpation revealed no signs of fluid thrill.

Investigations: Laboratory investigations revealed the following:

- **TSH levels:** 1400 uIU/l (normal: 0.35-5.5 uIU/ml)
- **T3 levels:** <2.5 ng/dl (normal: 100-200 ng/dl)
- **Thyroxine levels:** 1.35 µg/dl (normal: 5-12 µg/dl)
- **Beta-hCG, LH, and FSH:** within normal limits
- **CA-125, inhibin, dehydroepiandrosterone sulfate (DHEAS), testosterone, 17-hydroxyprogesterone, and insulin-like growth factor-1 (IGF-1):** all within normal limits
- **Tumor markers (CA-125, Human Chorionic Gonadotropin (HCG), 24-hour urine vanillylmandelic acid (VMA), and Alpha-fetoprotein (AFP)):** not elevated

These figures demonstrate after injecting 50 mL of non-ionic iodinated contrast intravenously, an abdominal contrast-enhanced CT scan was conducted. The results showed:

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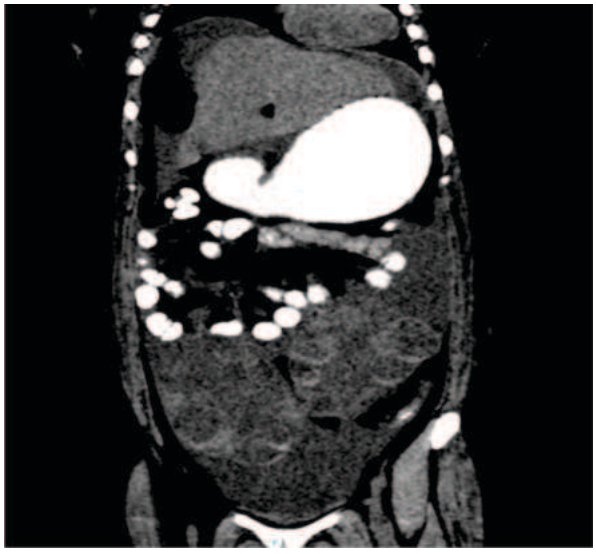
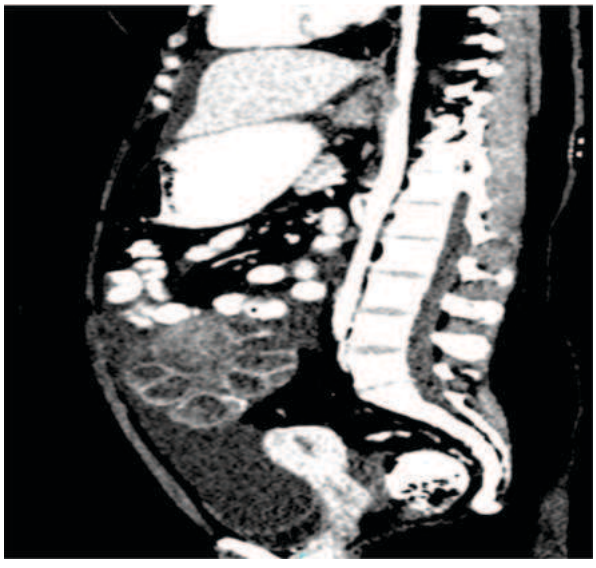
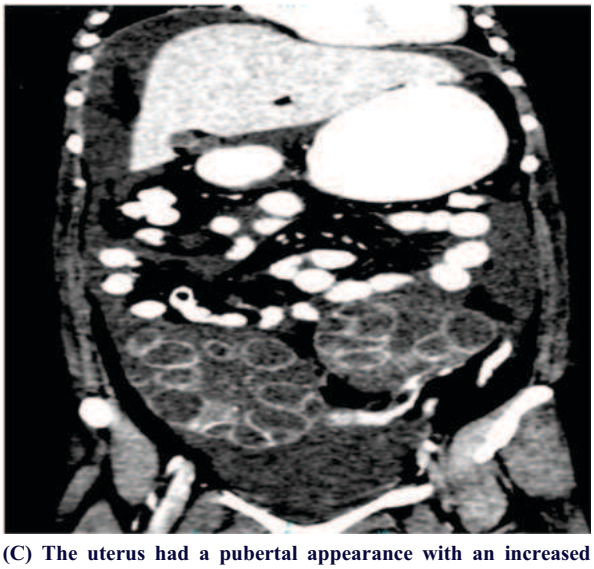


(A) A large cystic lesion occupying the entire pelvis with thin enhancing septae, but no fat, calcification, or solid components suggestive of malignancy.

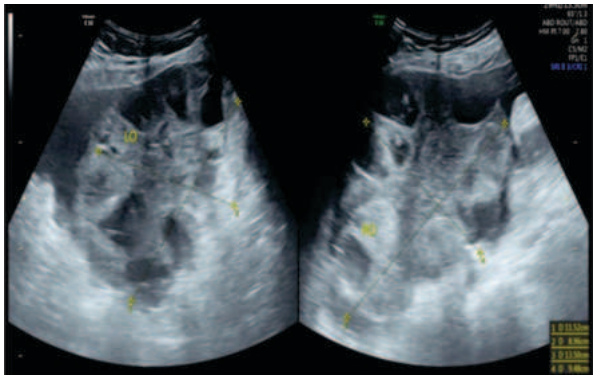


(B) Bilateral cystic lesions adjacent to the uterus, implying bilateral ovarian cysts with thin internal septations.

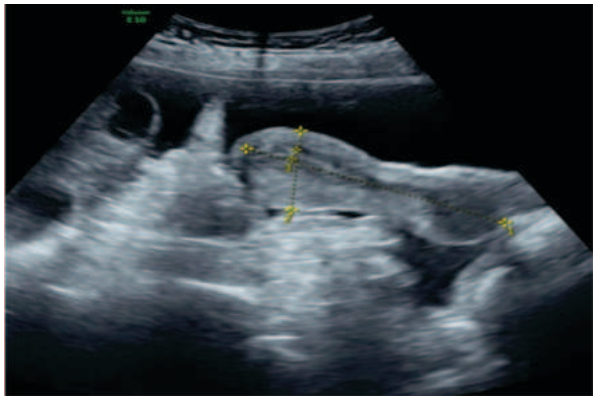


(C) The uterus had a pubertal appearance with an increased anteroposterior diameter, giving it a globular shape. The endometrial lining was well-demarcated.

These figures show Pelvic ultrasound in the parasagittal plane demonstrated:



(A). An enlarged uterus (10 x 7 x 4 cm) with a trilaminar endometrium, consistent with a post-pubertal appearance.



(B). Enlarged bilateral ovaries with multiple cystic lesions featuring thin internal septations. No vascularity was observed in the septae on Doppler ultrasound. There were no solid components, echogenic debris, calcification, or nondependent echogenic foci.

Diagnosis

The diagnosis of Van Wyk Grumbach Syndrome was determined in light of the clinical presentation, test findings, and imaging data. Bilateral multicystic ovaries and spontaneous ovarian hyperstimulation were most likely caused by the patient's hypothyroidism, which was shown by abnormally high TSH levels as well as low T3, thyroxine, and other thyroid secretions.

Management and Outcome

Levothyroxine replacement medication was initiated for the patient, with long-term monitoring scheduled. The ovarian cysts were not surgically removed since it was anticipated that they would go away with proper supplementation of thyroid hormone.

DISCUSSION

Even though it is uncommon, young girls who come with ascites, hypothyroidism, and ovarian cysts should be evaluated for Van Wyk Grumbach Syndrome. Regression of ovarian cysts can be achieved by treating hypothyroidism early on and avoiding needless surgical procedures. In order to prevent misdiagnosis and guarantee proper treatment, this case emphasizes the significance of a complete endocrine examination in patients with atypical ovarian tumors and premature puberty. In our case, a 14-year-old female presented with bilateral multi-cystic ovaries, abdominal distension, and profound hypothyroidism, which is consistent with the findings reported in the studies by Boddu et al.[7] and Purnamasari et al.[8]

In all three cases, patients demonstrated significant hypothyroidism, as evidenced by markedly elevated thyroid-stimulating hormone (TSH) levels. In our case, the TSH level was 1400 uIU/ml, similar to the levels observed in Purnamasari's patient (>1000 uIU/ml) and Boddu et al.'s cohort, where TSH levels ranged from >75 to 3744 uIU/ml. The consistently high TSH levels indicate the chronicity of untreated hypothyroidism, a hallmark of VWGS. Moreover, delayed growth, as seen in our patient and in Boddu et al.'s cases, highlights the critical

role of thyroid hormones in skeletal development.

In terms of clinical presentation, all three cases exhibited delayed bone maturation, short stature, and bilateral ovarian cysts. However, while our patient and those in Boddu et al.'s cohort showed symptoms like cold intolerance and fatigue, Purnamasari's case lacked these classic hypothyroidism symptoms. This variation in presentation highlights the broad clinical spectrum of VWGS and reinforces the need for a high index of suspicion, particularly when ovarian cysts and delayed growth coexist.

The misdiagnosis of ovarian malignancy is a frequent concern in VWGS, as noted in our case and Boddu et al.'s study, where several patients were initially referred for suspected ovarian tumors or surgical emergencies. In our case, the suspicion of malignancy led to a referral for a second opinion before the correct diagnosis of VWGS was made. Similarly, in Boddu et al.'s study, multiple patients were referred for surgical conditions such as ovarian torsion and abdominal masses. This underscores the importance of distinguishing VWGS from more severe pathologies through careful endocrine evaluation and imaging.

Treatment with levothyroxine led to significant clinical improvement in all cases. In our patient, as well as in Purnamasari's case, the ovarian cysts regressed completely following thyroid hormone replacement therapy, without the need for surgical intervention. Similarly, Boddu et al. reported that all patients, except those with ovarian torsion, were successfully managed with levothyroxine alone. This demonstrates that thyroid hormone replacement is highly effective in resolving the symptoms of VWGS, including ovarian hyperstimulation.

CONCLUSION

This case highlights how important it is to rule out Van Wyk Grumbach Syndrome when making a differential diagnosis in young girls who have hypothyroidism and ovarian cysts. When hypothyroidism is detected and treated early on, symptoms can totally resolve without the need for surgery.

Conflict of Interest: The authors confirm there are no conflicts of interest.
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Consent: Written informed consent was obtained from all participants and securely archived.
Ethical Approval: The study received ethical clearance, adhering to the required institutional protocols.

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