Open Access
Volume 7 Issue 3
Case Report Article

Journal of Pediatrics and Neonatal Medicine
ISSN: 2694-5983

PUBTEXTO

Van Wyk–Grumbach Syndrome in a Child: A Rare and Reversible Cause of Precocious Puberty

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Article Info

Article History:
Received: 05 July, 2025
Accepted: 08 July, 2025
Published: 11 July, 2025

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DOI: https://doi.org/10.36266/JPNM/215

Abstract

Van Wyk-Grumbach syndrome is characterized by a constellation of findings such as vaginal bleeding, multicystic ovaries, and delayed bone age due to long-standing untreated hypothyroidism in a prepubertal girl child [1]. We report a case of 10.2 years old girl child presented with abdominal pain and two episodes of vaginal bleeding. Surgery was planned due to multicystic ovaries and an elevated CA125 level. On evaluation, her TSH was elevated with low free T4, and she had typical features of hypothyroidism. Her LH was prepubertal with marginally high FSH. She was started on a thyroxine supplement and asked for a follow-up. Her TSH was normalized, along with the resolution of cysts. Identification of this rare entity is necessary to prevent unnecessary intervention.

Keywords: Van Wyk-Grumbach syndrome; Peripheral precocious puberty; Hypothyroidism; CA-125

Introduction

Van Wyk-Grumbach syndrome is a rare condition that arises due to the unopposed action of TSH on FSH receptors, leading to varied manifestations [1]. The elevated TSH directly stimulates FSH receptors, leading to precocious puberty. This is GnRH-independent precocious puberty, where the typical sequence of development is not maintained (i.e., the sequence of events is disrupted: Thelarche – Pubarche – Menarche). The enlarged ovarian cysts may be misdiagnosed as ovarian malignancy and subject the patient to unnecessary surgery.

Case Report

A ten-year-old, 2-month-old girl was referred for the fitness of ovarian tumour excision surgery. She complained of abdominal pain on and off for the last four to five months, with two episodes of vaginal bleeding. With these complaints, they consulted a gynaecologist one week back. Ultrasound of the abdomen showed multiple cysts in both ovaries. A hypoechoic cyst of size 9.4 × 8.2 cm with multiple internal septations was seen in the right ovary (Figure1). The left ovary showed a large, well, well-defined hypoechoic cyst of size 5.3× 3.9 cm with few septations. Her Cancer antigen (CA 125) level was 91 U/ml (normal: <35 U/ml), and her alpha-fetoprotein level was 3.1ng/ml (normal < 10 ng/ml). Based on the findings, the parents were counselled that such features are consistent with ovarian malignancy and that she needs urgent surgery. During her preoperative workup, Thyroid stimulating hormone (TSH) was 276 µIU/ml (normal range: 0.76-6.4 µIU/ml), and free T4 was 0.1 ng/dL (normal range: 0.9-1.7 ng/dL).

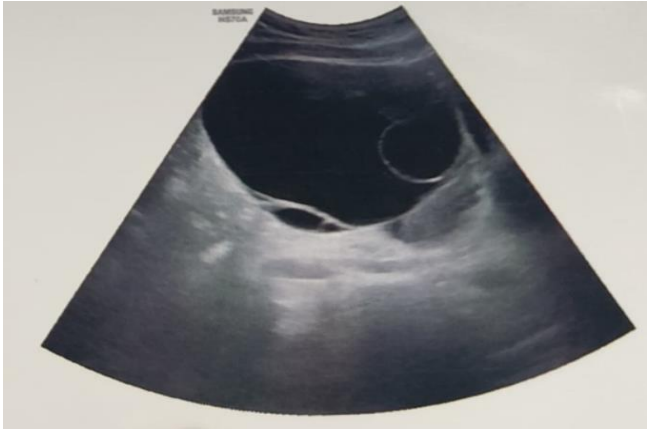

Figure 1: *Ultrasound of right ovary showing a cyst of size 9.4 × 8.2 cm with multiple internal septations.*

She appeared dull, with puffiness around her face. She was shorter than her peers, with average scholastic performance. She had other symptoms of hypothyroidism, such as dry skin, increased hair fall, and constipation. Her weight was 35 kg (50-75th centile), her height was 134 cm (25th centile), and her BMI was 19.5 kg/m^2 with

a standard deviation score (SDS) of -0.5. A swelling in the neck was noted, which moved with deglutition (Grade 2 goitre). The pubertal assessment revealed breast development (Tanner stage 2) in the absence of pubic or axillary hairs. Her bone age corresponded to 7 years (Greulich and Pyle's atlas). Her LH was 0.1 mIU/ml (normal: 0.1-6.0), and her FSH was 4.28 mIU/ml (normal: 0.3-2.0). These findings are consistent with isosexual peripheral precocious puberty. Based on the conglomeration of these symptoms, a diagnosis of Van Wyk-Grumbach syndrome was made. We prescribed her thyroxine 100 mcg per day and asked for a follow-up. She consulted us after 2 months with a TSH report of 1.9 µIU/ml, and an ultrasound of the abdomen showed complete resolution of the cysts. Her symptoms showed significant improvement.

Discussion

The onset of secondary sexual characteristics before 9 years in boys and 8 years in girls is termed precocious puberty [2,3]. Van Wyk-Grumbach syndrome can present as abdominal pain, vaginal bleeding, short stature, absence of pubic and axillary hairs, and lack of breast development in girls [4,5].

The exact mechanism of the development of precocious puberty is not known, but a lack of specificity in the feedback mechanism can lead to the overproduction of multiple hormones [4]. In very high concentrations, TSH cross-reacts with FSH receptors due to structural homology, leading to hyperplasia of ovarian follicles and increased production of oestradiol [6]. The ovarian enlargement can be due to myxomatous infiltration [8].

In the case of our patient, she was posted for surgery due to the large ovarian size and elevated CA-125 levels. CA-125 levels can be seen in various non-malignant conditions [7]. The cysts completely resolved with the normalization of TSH. Her parents noticed an improvement in her external appearance and concentration in her studies.

Conclusion

We could prevent unnecessary surgery by correctly identifying the condition. The presence of palpable mass with isosexual precocious puberty would suggest ovarian malignancy, but if bone age is delayed, then we should think of VWGS [8]. This case highlights the importance of the hormonal evaluation in precocious puberty.

Statements and Declarations

Funding: None

Ethical Declarations

Conflicts of Interests: None

Author's Contribution: All authors contributed equally to the preparation and review of this manuscript.

Acknowledgment: None

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