Case Report

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Van Wyk Grumbach Syndrome: A Rare Cause for Ovarian Cyst and Precocious Puberty in Children

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ABSTRACT

Van Wyk Grumbach syndrome (VWG) is a rare syndrome characterized by precocious puberty, hypothyroidism, delayed skeletal maturation and bilateral ovarian cysts. A case of 6-year-old girl who presented with vaginal bleeding and pain in abdomen is reported. She was diagnosed with multicystic ovarian cysts in bilateral ovaries on ultrasound and uncontrolled hypothyroidism. This case highlights the importance of doing thyroid function test in children who presents with bilateral ovarian cysts along with precocious pregnancy to make a diagnosis of this rare syndrome and avoid unnecessary surgical intervention.

Keywords: Precocious puberty, Ovarian cysts, Hypothyroidism, Delayed skeletal maturation.

INTRODUCTION

Van Wyk Grumbach syndrome (VWG) is a rare syndrome first described by Van Wyk and Grumbach in 1960. It is characterized by iso-sexual precocious puberty, multi-cystic ovary and uterine bleeding along with primary hypothyroidism.[1]

CASE DESCRIPTION

A 6-year-old girl, presented in gynecology emergency with complaints of bleeding per vaginum and pain abdomen for one month. Initially bleeding was in the form of spotting which later increased to soaking one pad per day for past one week. It was associated with dull aching pain in lower abdomen for past one month. She had history of constipation on and off for past two months. There was no history of any trauma, sexual abuse, burning micturition, headaches, visual disturbances, vomiting and head trauma. She was born of non-consanguinity with normal birth and development. Her parents were of normal height and weight. Family history was unremarkable.

Prior to admission at our hospital caregivers were seeking medical advice from the local practitioners. Her USG abdomen had reported complex ovarian cysts of size approximately 6 cm × 4 cm in both ovaries, for which she was referred to our hospital for surgical management.

On examination, she had short stature (98 cm) while her weight (17 kg) and occipito-frontal circumference (51 cm) were appropriate for age. She had mild pallor, coarse facial features, dry skin and large tongue. She had no pedal edema and no thyroid swelling (Fig. 1). Tanner staging showed breast development stage 1 with no pubic and axillary hairs. Abdomen was soft, mild tenderness was present in lower abdomen, no mass, no guarding, rigidity and organomegaly. Rest of the systemic examination was unremarkable.

Local examination showed bleeding per vaginally, hymen intact, no signs of trauma. Per vaginum examination was not done. Per rectal examination

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Fig. 1: 6-year-old girl with VWG Syndrome with coarse facies

revealed small sized uterus with bilateral adenxal masses of size 5 cm × 5 cm, rectal mucosa free. Orthopedic consultation was done to rule out any spine abnormality.

Laboratory investigations showed hemoglobin = 9 gm%, Follicular stimulating hormone (FSH) = 7.8 mIU/mL (normal 0.5-2 mIU/mL) free T3 = 0.01 pg/mL (normal range 1.4-4.2 pg/mL), free T4 = 0.01 ng/dL (normal range 0.8-2 ng/dL), Thyroid stimulating hormone (TSH) levels were greater than 1500 micro IU/mL (normal range 0.35-5.5 micro IU/mL), suggestive of severe hypothyroidism. Anti TPO antibodies were positive. Bone age was delayed (3 years). Her anti-tissue transglutaminase antibody levels were normal. Ultrasound neck reported normal thyroid gland. Ultrasound pelvis revealed uterus size 6.8 cm × 3.0 cm × 2.5 cm, complex bilateral ovarian cyst of size 6.3 cm × 3.2 cm with normal blood flow in both ovaries and no evidence of torsion. MRI of the patient could not be done due to financial constraints.

Based on clinical features of bleeding per vaginum, short stature, blood investigation showing hypothyroidism and imaging reporting bilateral complex ovarian cyst, diagnosis of Von Wyk Grumbach (VWG) syndrome was considered. Patient was started on thyroxin replacement therapy after endocrinology consultation. Parents were counseled regarding need for medical management and regular follow-up. On further follow-up after 6 months, her vaginal bleeding had resolved, the size of ovarian cysts size was reduced and serum TSH level came to normal.

DISCUSSION

Profound chronic hypothyroidism has been associated with delayed linear bone growth, isosexual pseudoprecocious puberty and bilateral ovarian cyst. All these findings collaborated in a condition called Van Wyk Grumbach syndrome. As clinical and laboratory profile of our patient was similar so diagnosis of VWG syndrome was made.

VWG syndrome is a rare syndrome. Its exact incidence is not known. A retrospective review of 33 pseudoprecocious puberty patients over 10 years had reported profound hypothyroidism in 24% of cases.[2] Only a handful of VWG syndrome cases have been reported till date especially from low and middle income countries.[3-6]

The explicable pathophysiology suggested is profound hypothyroidism (usually autoimmune in origin) leading to TSH surge. Due to structural analogy between subunit of glycoprotein receptor of TSH and FSH, elevated TSH causes elevated FSH and thus high estradiol levels. Elevated FSH and estradiol levels when acts on ovaries and breast leads to multicystic ovaries, uterine bleeding and breast enlargement. More-so-over chronic profound hypothyroidism leads to poor bone growth and neurodevelopment.

The diagnosis can be established by typical phenotypic features supplemented with imaging finding of ovarian cyst and hypothyroidism. Management is usually supportive. Majority of the clinical features reverse after thyroid supplementation including ovarian cysts. In our case also after thyroid hormone supplementation vaginal bleeding stopped and ovarian cysts regressed. Early diagnosis improves the prognosis.[2]

CONCLUSION

VWG syndrome is an important treatable cause of precocious puberty that should be kept in mind while investigating cases of precocious puberty. Timely done thyroid function tests and prompt diagnosis of VWG syndrome can reverse the symptoms and may alleviate the need of surgical intervention.

Source of Support

Nil

Conflict of Interest

There are no conflict of interest.

Financial Disclosure

None

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Nil

Ethical statement: Written informed consent was taken from patient's parents regarding publication of this case report.

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