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Case Report

Decoding the ovary-thyroid connection: a case report on intricacies of untreated hypothyroidism

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ABSTRACT

Precocious puberty may be a rare presentation of untreated hypothyroidism, while delayed puberty is its norm. Van Wyk-Grumbach syndrome (VWGS) refers to the development of isosexual precocious pseudo puberty and multicystic enlarged ovaries in the presence of hypothyroidism. Here we report a case of an eight-year-old girl child who required emergency surgical intervention attributable to the aforementioned syndrome.

Keywords: Hypothyroidism, Precocious puberty, Ovarian cyst, Thyroxine, Van Wyk-Grumbach syndrome

INTRODUCTION

Children with hypothyroidism usually present with delayed growth and development, but on rare occasions can present with signs of precocious puberty and ovarian cysts. This presentation is called Van Wyk-Grumbach syndrome (VWGS).[1] VWGS was first described in 1960 as a syndrome of juvenile hypothyroidism associated with pubertal advancement.[2] Acquired pediatric hypothyroidism is most commonly caused by chronic autoimmune thyroiditis and occurs in 1.3–4% of children.[3]

There are various theories to explain the mechanism of the development of symptoms in these patients. According to van Wyk and Grumbach, the pituitary hypothalamic axis overproduces gonadotropins and other hormones including estradiol due to lack of specificity of the feedback system which in turn causes the cystic enlargement of ovaries.[2] Sometimes these ovaries became very huge in size and may end up in torsion and can compromise the fertility of the patient.

This case report underscores the potential for timely detection and early introduction of a single agent ‘thyroxine’ to prevent such complications.

CASE REPORT

An 8-year-old girl, second child of non-consanguineous marriage, with normal antenatal and postnatal history, presented with complaints of diffuse abdominal pain of one-week duration. On examination, she was obese with body mass index (BMI) of 24.5 kg/sq.m with acanthosis nigricans, bilateral thelarche corresponding to Tanner stage B2P1. Her height was at -1.85 SDS and weight at +1.56 SDS as per World Health Organization (WHO) growth chart. Thyroid gland was normal in size clinically. Her abdomen was distended and showed severe right iliac fossa tenderness.

Blood investigations showed elevated thyroid stimulating hormone (TSH) with very low free T4 and free T3 levels. Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) values were prepubertal with estradiol level in pubertal range which was suggestive of peripheral precocious puberty. Ultrasound abdomen revealed bilateral enlarged ovaries with 'multiple cysts and features of right ovarian torsion (Figure 1). Thyroglobulin antibody was 931.5 IU/ml and was indicative of autoimmune thyroid disease.

Table 1: Blood investigation on admission.

Investigations	Values	Indications
Free T4 (ng/dl)	<0.015	Very low
TSH (microU/ml)	751.4	Very high
Thyroglobulin antibody (IU/ml)	931.5	Very high
LH (miu/ml)	0.17	Prepubertal
FSH (miu/ml)	3.22	Prepubertal
Estradiol (pg/ml)	29	Pubertal
Hemoglobin (g/dl)	8.6	Low

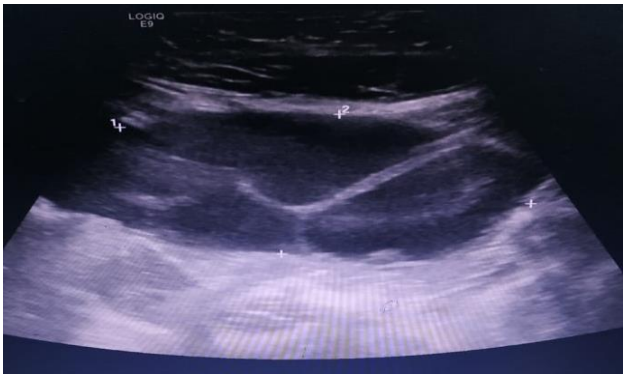

Figure 1: USG abdomen showed bilateral complex ovarian cysts.

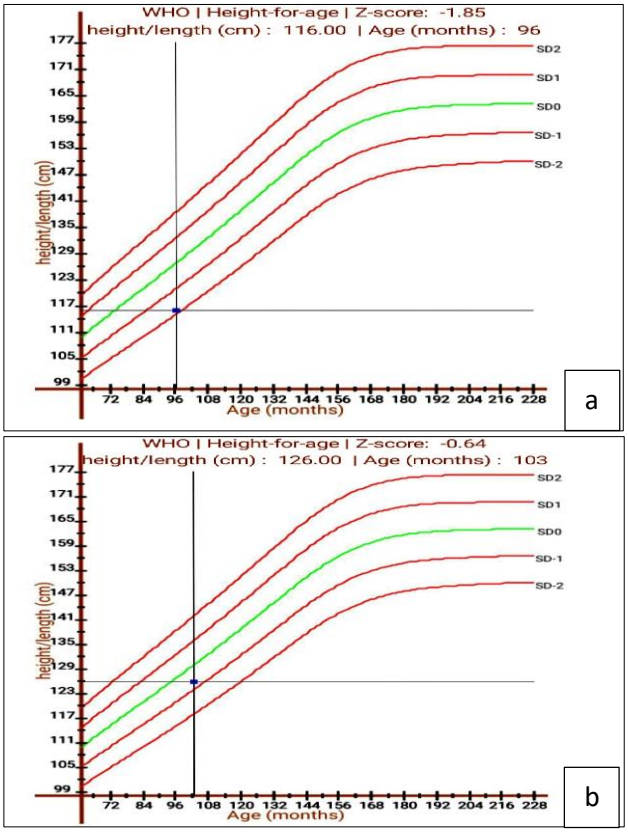

Figure 2 (a and b): Comparison of height before and after starting levothyroxine.

She was immediately started on levothyroxine initially at a lower dose 25 mcg and was gradually titrated up, in accordance with the clinical and biochemical parameters. She underwent emergency laparotomy and right salpingo-oophorectomy with left ovarian cyst puncture. Post-operative period was uneventful. There was marked improvement in clinical parameters, ovarian cysts disappeared and she caught up with her height also (Figure 2). She started to perform school activities enthusiastically along with improvement in social interactions.

DISCUSSION

Acquired hypothyroidism is a relatively common endocrine disorder among children and early recognition is important to prevent serious complications like VWGS. Hypothyroidism usually manifest as excessive sleepiness, lethargy and constipation. But in rare occasions, it can present as peripheral precocious puberty, the VWGS. Girls present with premature menarche preceded by a brief period of thelarche while in boys this leads to macroorchidism without virilization.[4]

Short stature and delayed bone age can further help to point towards the diagnosis of above condition as other causes of precocious puberty usually are associated with accelerated growth velocity and advanced bone age.[1] VWGS is the only form of precocious puberty in which the bone age is delayed and this is due to long standing hypothyroidism.

The complex interactions within the hypothalamic pituitary axis play the key role in the development of VWGS. In addition to the theory postulated by van Wyk and Grumbach certain other hypothesis also exist. First, the TSH has the ability to weakly stimulate FSH receptor without stimulating LH receptor simultaneously which will point towards the low level of LH (pre-pubertal) in these patients.[5] Thus, with high TSH level, FSH receptors of ovary are stimulated due to molecular mimicry producing high amount of estrogen which causes bilateral enlargement of ovary and onset of menarche.[6] Second, the FSH secretion is stimulated by a constant high level of thyrotropin releasing hormone (TRH) which leads to development of clinical symptoms of VWGS.[7]

Laboratory investigations reveal very high level of TSH, prolactin, 17-β estradiol with suppressed levels of gonadotropins. The occurrence of VWGS can be easily prevented by the timely initiation of levothyroxine ‘the game changer’.

Due to lack of knowledge and unavailability of many published reports regarding this condition, there are higher chances of unnecessary surgical interventions and subsequent complications. Thus, primary hypothyroidism must be excluded in any girl child presenting with bilateral ovarian cysts with periodic per vaginal bleeding.

CONCLUSION

This case highlights how crucial it is to identify hypothyroidism as the reason of peripheral precocious puberty, particularly in children of short stature, as it can be easily treated with levothyroxine to avoid needless surgery.

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