

CASE REPORT

Case of Van-Wyk Grumbach syndrome

Vishnu Vasudevan, Arun Viswanath, Riaz Ahmad Misgar

Department of Endocrinology, Sher I Kashmir Institute of Medical Sciences, Srinagar, India

ABSTRACT

Background: Hypothyroidism in childhood typically leads to delayed puberty, rarely can it cause precocious puberty - this latter complex is eponymously known as Van Wyk-Grumbach syndrome.

Case description: We report a case of a seven and a half year old girl who was referred with vaginal bleeding after after starting her on levothyroxine replacement therapy for newly detected primary hypothyroidism. This case report illustrates the typical features of this rare syndrome for primarily educational purposes. Many case reports of Van Wyk-Grumbach syndrome have been published in world literature over the past seven decades after the initial description. Though the features of this syndrome are fairly well described in the literature, the understanding of pathophysiological mechanisms is speculative and still evolving.

Clinical relevance: Wide spread awareness of the syndrome will encourage primary physicians and paediatricians to counsel the family of a child before starting treatment for hypothyroidism which will help avoid unnecessary worry and more importantly inadvertent procedures or intervention.

JMS: 2020; 23(3):33-35 DOI: <https://doi.org/10.33883/jms.v23i3.777>

INTRODUCTION

Van Wyk and Grumbach first described this eponymous syndrome 60 years back as an association of hypothyroidism with precocious puberty (PP) and ovarian mass.¹ They mentioned it as an example of hormonal overlap in pituitary feedback; which is still an accepted pathophysiological mechanism for this peculiar syndrome. It causes gonadotropin independent iso-sexual precocious puberty and manifests as such in female children; males may be affected too causing macroorchidism. Thyroid hormone replacement causes reversal of almost all of the manifestations and it is crucial to consider this possibility in a girl child presenting with breast enlargement, adnexal mass or menstrual bleeding at an earlier age than normal.²

Here we describe a girl child who was referred to our endocrinology out-patient department with menstrual bleeding after starting treatment for hypothyroidism.

CASE REPORT

A 7 years and 4 months old girl was referred to our endocrine OPD with vaginal bleed since 4 days. She was from a poor socioeconomic background, the product of a non-consanguineous marriage, third in birth order and was born at term after an uneventful antenatal period. Her birth weight is unknown but as a new-born she was hospitalized for 3 days for some feeding difficulties (details unavailable). There is no history of prolonged jaundice, hypoglycaemia, seizures, umbilical hernia, constipation or hypotonia. She was breastfed till 2 years and achieved all milestones at appropriate age. She was apparently normal

Correspondence:

Dr Raiz Ahmad Misgar,
Associate Professor, Department of Endocrinology, SKIMS
Email: drreyaz07@rediffmail.com

Access this article online



Website:
www.jmsskims.org

DOI:
<https://doi.org/10.33883/jms.v23i3.777>

How to cite this article: Vasudevan V, Viswanath A, Misgar RA. Case of Van-Wyk Grumbach syndrome. JMS 2020; 23(3):33-35

Received: 2020-08-26 Accepted: 2020-09-09



This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

till 5 years of age when she started with progressive lethargy and slowness of movements. She stopped playing and used to remain in the kitchen for most part of the day. She also developed poor appetite, constipation and puffiness of face for the past 1 year. Her scholastic performance remained average. She was evaluated by a local physician and was advised thyroid function test revealed total T4 of <0.3 mcg/dL and TSH > 150mIU/L. Patient was started on levothyroxine 100mcg tablet. One day after starting levothyroxine she developed vaginal bleeding and was thus referred.

The child was short; she had a puffy face and thick skin. She had no thyromegaly, café-au lait macules or skeletal deformities. She had a pulse rate of 88 beats per minute, regular and normal in volume and character. Her anthropometry revealed height of 106cm (-3.0 SDS; Height age of 5 years), target height SDS was -0.7, and weight of 21 kg (-0.5 SDS). Her arm span was 99cm, US/LS were 53cm/53cm. OFC was 51cm. She had an SMR of B2P1 with no axillary hair. Other systemic examination was unremarkable. There was no delay in tendon reflexes. Her investigations revealed a hemoglobin of 9.4 g%, MCV was 93fL, MCH was 29, TLC was 5,200/mm³, platelet count was 3.17 lakhs, serum total cholesterol was 174mg/dL, triglycerides were 157mg/dL, blood urea 31mg%, serum creatinine 0.56mg%, LFT was normal. The creatinine kinase level was 269, LDH was 377, uric acid was 4.2mg%, serum calcium was 9.47mg%. Hormone profile revealed LH 0.4 IU/L, FSH 3.54 IU/L, Prolactin 54.46 ng/mL, E2 47 pg/ml, 8AM cortisol 8.58 mcg/dL, Total T3 2.20 ng/mL, Total T4 16.7 mcg/dL, TSH 9.31 mIU/L, AntiTPO Ab 370.5 IU/L. X ray knee did not show any epiphyseal changes. Bone age was delayed (Greulich and Pyle method) 3 years (BA << HA < CA). USG pelvis revealed bilateral ovaries showing multiseptate cysts, right ovary volume of 14 cc, left ovary volume of 40cc, endometrial thickness was 4mm, size of the uterus was 5.3x1.8x2.7 cm with an ellipsoid volume of 12.9 mL. USG thyroid revealed that the right lobe of the thyroid was 7*8*16 mm and left lobe was 5*7*10 mm with a heterogeneous echopattern. A final diagnosis of Juvenile autoimmune thyroid disease with primary hypothyroidism and peripheral (GnRH-independent) precocious puberty (Van Wyk -Grumbach Syndrome) was made. The child was asked to continue treatment with 100mcg of levothyroxine and the parents

were reassured. After one year of treatment and follow up, the child is doing well and has not had any further bleeding per vaginum. She has grown in height, her breast regressed to B1 and she also reduced her weight.

DISCUSSION

The eponymous Van Wyk-Grumbach syndrome is one of the most puzzling, yet interesting pediatric complexes. Clinical pointers to differentiate it from true (GnRH dependent) precocious puberty include first; thelarche and menarche without pubarche, second; short stature as opposed to increased height velocity in GnRH dependent PP, and third; delayed bone age compared to height age and both less than chronological age as illustrated in this case.³ LH is prepubertal as is expected in any etiology of GnRH independent PP. It also exemplifies a situation which needs masterly inactivity on the part of the clinician, as the multicystic ovaries found in this condition is important to recognise as a part of this syndrome and thus unnecessary investigation or inadvertent surgical management should be avoided. Also if an MRI (magnetic resonance imaging) of the brain is done as part of evaluation of precocious puberty, it is likely to show a sellar mass which is also to be expected here; but the unwary might seek a neurosurgery consult. This condition incorporates points pertinent to TSH and FSH interaction; it is an example of "hormonal overlap" or "specificity spillover" where high levels of TSH (as in our case) stimulate the FSH receptors in the ovarian granulosa cells to produce estrogen. The role of prolactin in mammary gland and ovary development and physiology has also been postulated as a potential mechanism. Our case illustrates the situation where menstrual bleed happens after the start of treatment for chronic acquired severe hypothyroidism.⁴ It may be prudent to convey this to the parents of such children beforehand, to allay their anxiety later. Also it could be debated whether starting with a lower dose of levothyroxine and slow up-titration might prevent such a sequel in children presenting with a similar clinical picture.⁵

REFERENCES

- [1] Wyk JJV, Grumbach MM. Syndrome of precocious menstruation and galactorrhea in juvenile hypothyroidism: an example of hormonal overlap in pituitary feedback. *J Pediatr* 1960;57:41635.
- [2] Sanjeevaiah AR, Sanjay S, Deepak T, Sharada A, Srikanta SS. Precocious puberty and large multicystic

- ovaries in young girls with primary hypothyroidism. *Endocr Pract* 2007;13:6525.
- [3] Reddy P, Tiwari K, Kulkarni A, Parikh K, Khubchandani R. Van Wyk Grumbach Syndrome: A Rare Consequence of Hypothyroidism. *Indian J Pediatr* 2018;85:102830.
- [4] Zhang H, Geng N, Wang Y, Tian W, Xue F. Van Wyk and Grumbach syndrome: Two case reports and review of the published work. *J Obstet Gynaecol Res* 2014;40:60710.
- [5] Tran S, Kim EE, Chin AC. Severe menorrhagia, unilateral ovarian mass, elevated inhibin levels, and severe hypothyroidism: An unusual presentation of Van Wyk and Grumbach syndrome. *J Pediatr Surg* 2013;48.