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CASE REPORT

Van Wyk Grumbach Syndrome: A Case Report and Review of Literature

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Introduction

Van Wyk Grumbach syndrome refers to a conglomeration of hypothyroidism, pre-pubertal vaginal bleeding, multi-cystic ovaries and delayed bone age in case of females. The pathophysiology of this syndrome can be varied with multiple hormone interactions.

Multi-cystic ovaries, ovarian enlargement and vaginal bleeding in young adolescent girls can be a cause of concern with clinicians overdoing investigations and surgeries. Prompt initiation of thyroxine replacement can resolve symptoms and restore growth in these children [1].

Here, we report the case of a 8 year old girl presenting with vaginal bleeding and subsequently diagnosed as Van Wyk Grumbach Syndrome.

Case Report

A girl aged 8 years 5 months presented with complaints of vaginal bleeding since 6 days. Bleeding was scanty, brownish, non-odorous with occasional lower abdomen pain. There was no history of trauma, foreign body insertion or sexual abuse. No significant medical, surgical or family history was noted.

On examination, she was alert with weight of 29 kg(10th centile), height 119 cm(25th centile), BMI 20.5 and arm span 120 cm. Neck examination showed no goitre or lymphadenopathy. She had breast development at Tanner stage 2, with absent axillary and pubic hair. Abdomen was soft. External genitalia and pelvic examination (inspection) was normal with slight brownish discharge through hymen.

Ultrasound already done at another centre showed normal kidneys, uterus 5.6×2.5×3.0 cm, ET 4.5 mm and bilateral enlarged multi-cystic ovaries (volume, size not mentioned) with minimal free fluid in pelvis.

Investigations showed microcytic anaemia—Hb 10.5 g/dl, TSH 1058 µIU/mL, FSH 4.8 mIU/mL, LH 0.1 mIU/mL, Prolactin 61 ng/mL, E2 116 pg/mL, CA125 33 U/mL, B Hcg 0.4 mIU/mL, AFP 1.3 IU/mL, CEA 1.76 ng/mL and anti-TPO antibody elevated at 67.54 IU/mL.

MRI pelvis revealed uterus 5.8×2.2×2.8 cm, ET 3.4 mm, bilateral adnexal cystic lesions with thin septae measuring 7.5×4.8×4.8 cm on right side and 6.7×3.1×4.2 cm on left side. Minimal free fluid was seen in pelvis (Fig. 1).

X-ray of her left hand for skeletal age showed delayed bone age of 6–7 years.

The diagnosis was consistent with primary auto immune hypothyroidism and opinion of endocrinologist was sought. She was started on 75 mcg thyroxine supplementation. On follow-up, at 6 weeks TSH was 0.3 µIU/ml and hence dose of thyroxine was titrated. On 3-month follow-up, ultrasound showed resolution of ovarian cysts and with a catch up of growth (Fig. 2). At the time of writing this case report, the patient has completed her 1-year follow-up, her height was 135 cm(> 50thcentile) and weight was 35 kg(> 50 th centile).

Discussion

Primary hypothyroidism is usually associated with growth and pubertal delay. Judson J.Van Wyk and Melvin M. Grumbach in 1960 described a syndrome associated with juvenile hypothyroidism, the cardinal feature of which is sexual

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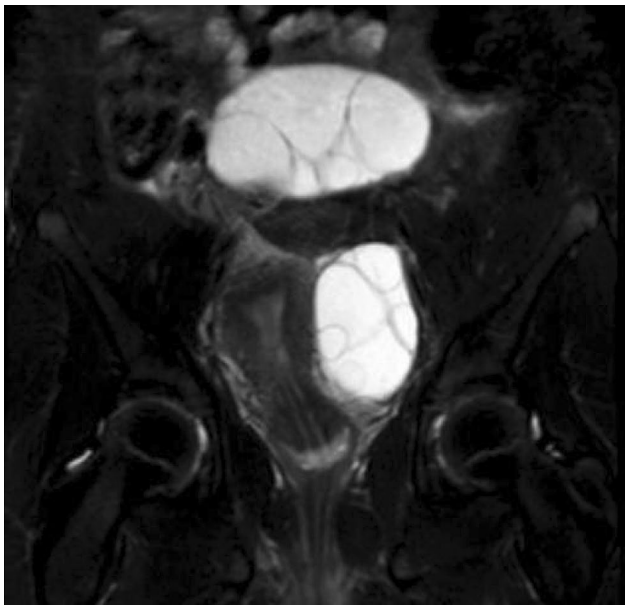

Fig. 1 MRI showing enlarged cystic ovaries

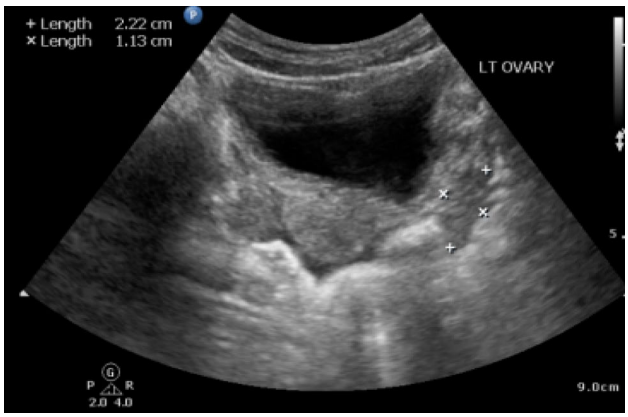

Fig. 2 Ultrasound image showing resolution of ovarian cysts

development beyond that consistent with the bone age and other indices of maturity and this was later named as Van Wyk Grumbach syndrome.

Complex interactions between different hypothalamic–pituitary axes seem to be the driving factor for Van-Wyk Grumbach syndrome. Hormonal overlap in the pituitary feedback mechanism, with both TSH and gonadotrophins being glycoproteins and lack of specificity at the hypothalamic level, was originally postulated. TRH-induced TSH excess stimulating the gonadal FSH receptors explains the clinical phenotype with isosexual precocious puberty (breast development and menstruation) and multi-cystic ovaries [2]. On the contrary, TRH-induced hyperprolactinemia suppresses the pituitary gonadotrophic axis and LH in particular. Pubic and axially hair are absent due to absence of adrenal androgens.

Girls in the peri-pubertal period when their FSH levels are low are usually affected. Also, the response of the FSH receptors to TSH seems to be dose-dependent as only children with very high levels of TSH seem to be affected. (Studies have shown that recombinant TSH can interact with the human FSH receptor at higher doses only.)

Multi-cystic ovaries may be due to elevated gonadotrophins or increased sensitivity to low or normal gonadotrophins. In previous reports, histopathological analysis of resected ovaries and ovarian cysts showed cystic follicles with minimal luteinization. Some reports also suggest myxedematous infiltration of ovaries.

Presentation of isosexual precocious puberty with large multi-cystic ovaries could suggest ovarian tumours, but the main differentiation factor seems to be the delayed bone age. It is important for all girls with this presentation to undergo evaluation for hypothyroidism. Treatment with thyroxine can reverse all the symptoms and the ultrasound appearance as was demonstrated in our case.

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Declarations

Conflict of interest The authors declare that there are no conflicts of interest.

Ethical approval The institutional ethical committee approval had been obtained for publishing the case report.

Informed consent Written informed consent for publishing the case report had been obtained from the father of the minor patient.

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